# DISSEMINATED SCLEROSIS.

BY

ARNOLD EDWARDS, M.B.,

RESIDENT MEDICAL OFFICER TO THE CHORLTON-UPON-MEDLOCK DISPENSARY, MANCHESTER;
LATE SENIOR HOUSE-SURGEON TO THE LEEDS GENERAL INFIRMARY; LATE
HOUSE-SURGEON TO THE MANCHESTER SOUTHERN HOSPITAL.

WITH ILLUSTRATIONS.

JOHN HEYWOOD,
DEANSGATE AND RIDGEFIELD, MANCHESTER.
2, AMEN CORNER, LONDON, E.C.
22, PARADISE STREET, LIVERPOOL.
33, BRIDGE STREET, BRISTOL.


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JOHN HEYWOOD,
Deansgate and Ridgefield, Manchester;
2, AMEN CORNER, LONDON, E.C.;
22, Paradise Street, Liverpool;
33, Bridge Street, Bristol.

# PREFACE.

In writing the following pages I have had occasion to utilise the opportunities for clinical work available at the various Manchester hospitals—notably the Manchester Royal Infirmary. With the exception of one case of my own, I am entirely indebted to the Physicians of these institutions for the kindness and courtesy with which they have placed cases at my disposal.

I desire to especially acknowledge my great indebtedness to Professor Dreschfeld for permission to work in his laboratory and for the use of much clinical and pathological material; to Dr. Bury for numerous cases and the brain and spinal cord of Case VI.; to Drs. Steell, Harris, and Reynolds for liberty to report cases; and to my friend Dr. Williamson for repeated acts of kindness.

The Illustrations are from drawings, executed by myself from pathological specimens the more interesting of which accompany the thesis.

ARNOLD EDWARDS.

Manchester,

*February, 1895.*

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# DISSEMINATED SCLEROSIS.

## INTRODUCTION.

DISSEMINATED SCLEROSIS is a disease characterised pathologically by numerous scattered patches of sclerosed tissue distributed irregularly throughout the nervous centres; clinically by various symptoms, the most characteristic of which are "intention tremor" affecting the different parts of the body, a peculiar difficulty of articulation, nystagmus, an insidious paralysis with contraction principally of the lower limbs, and impairment of the mental powers.

It is somewhat notable that such a remarkable disease as that under discussion should have escaped the eye of the physician until about the middle of the present century. We may assume as responsible for this, the facts that a morbid process presenting so commonly anomalous features must frequently have led neurologists into error; and that the lingering and hopeless nature of the disease usually precluded the sufferer remaining in hospital until the end—the pathological key to the patient's condition was thus lost from the absence of a *post-mortem* examination.

To France belongs the honour of primarily drawing attention to the disease, since it was Cruveilhier who first described the pathological appearances and a few of the clinical features of what he termed "grey degeneration" in his "Atlas" published between 1835—1842. Carswell also depicted similar lesions in his "Atlas" in the year 1838, his cases being, like the foregoing,

drawn from Parisian hospitals. For several years subsequent to this, French writers appear to have taken but a desultory interest in the subject, and the Germans were the next to resume the thread of investigation. In 1855 Türck referred to analogous cases, and various data relating to the elucidation of the disease were subscribed by Frerichs, Valentiner, and others. In 1862 Gallic enthusiasm revived, and Charcot and Vulpian undertook elaborate research at the Salpêtrière, with the result that disseminated sclerosis took its place among recognised diseases of the nervous system.

Charcot declared in 1868 that disseminated sclerosis was unknown in England, and he was unfortunately correct, for there is no record of the disease in this country until 1873, when Moxon published a case in the *Lancet*.

# CHAPTER I.

## ETIOLOGY OF DISSEMINATED SCLEROSIS.

IT is convenient to divide the causes of the disease into predisposing and exciting.

### PREDISPOSING CAUSES.

*Sex.*—From an investigation of 33 undoubted cases of disseminated sclerosis which I have collected, and on which the observations in the following pages are largely based, I find that 23 out of the 33 cases are males and only 10 are of the other sex. Again, a perusal of the reports of 60 published cases, in which either typical symptoms were present or autopsies revealed the disease, resulted in the males still taking the lead, numbering 39, as against 21 females. Charcot[1] has stated that the disease is commoner in women, his first 34 cases being made up of 25 females and 9 males. It must, however, be remembered, in considering the value of Charcot's statement, that females largely predominate in the clinics of La Salpêtrière. Moncorvo[2] also out of a total of 21 cases notes 12 girls to 9 boys, and Erb[3] gives the ratio as 5 to 4 in favour of the women. Gowers[4] thinks that disseminated sclerosis occurs in both sexes with nearly the same frequency. Chvostek's[5] 16 cases included only 6 women, and Marie[6] has collected 14 examples of the disease in childhood, consisting of 8 boys and 6 girls. Finally, in the practice of Spitzka,[7] of 22 cases only 7 were females.

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[1] "Lectures on the Diseases of the Nervous System." New Sydenham Society, 1887, No. VIII., p. 219.

[2] *União Med.*, Rio de Jan., 1884, IV., p. 16.

[3] "Ziemssen's Cyclopædia of the Practice of Medicine," Vol. XIII., 1878, p. 475.

[4] "Diseases of the Nervous System," Vol. II., 1888, p. 507.

[5] *Wien. med. Pr.*, 1873.

[6] *Rev. de Méd.*, Paris, 1883, III., p. 536.

[7] "Pepper's System of Medicine," Vol. V., 1886, p. 885.

*Age.*—Disseminated sclerosis may be met with at almost any period of life, but in old age is extremely rare. Charcot[1] has said that the disease rarely shows itself after 30, and that the age of 40 was the outside limit to which patients attacked by disseminated sclerosis attain. Erb[2] thinks it is very seldom, if ever, seen after 45, and Marie[3] considers that disseminated sclerosis may be almost eliminated if the disease begins after the fortieth year. The oldest undoubted case on record seems to be that of a patient of Strümpell's,[4] in whom the symptoms began at the age of 60; this was verified by *post-mortem* examination. Bastian[5] gives the case of a man in whom signs of the disease appeared when he was over the age of 50; this patient died at 62, and the autopsy confirmed the diagnosis. Kirkland[6] quotes the case of a woman of 75 with typical symptoms of disseminated sclerosis, and Dercum[7] reports an example of the disease in which the earliest symptoms began at 57; but these cases were not corroborated by autopsy. Among my cases is a man who first showed signs of disseminated sclerosis at the age of 44; the patient is now 50, and presents symptoms of the advanced disease. Charcot's[8] earliest case was a child of 14, and the older teaching was that disseminated sclerosis was essentially a disease of adult life. This is being refuted by an increasingly large number of cases reported as developing in children. Pritchard,[9] in a recent search through the literature of the subject, has collected 60 cases of the disease in children, their ages ranging from 14 months to 14½ years. Totzke[10] also has got together 31 cases of disseminated sclerosis in children, and of these 19 began before the sixth year and 12 between six and fourteen years. Oppenheim[11] has stated that many cases

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[1] *Loc. cit.*, p. 219.

[2] *Loc. cit.*, p. 475.

[3] "Les Maladies de la Moelle," Paris, 1892.

[4] "Text-book of Medicine," 2nd American Edition, 1893.

[5] *Clinical Society's Transactions*, London, 1884, Vol. XVII., p. 7.

[6] *Brit. Med. Jour.*, March 3, 1893.

[7] *International Clinics*, 1894, Vol. I., S. 3, p. 122.

[8] *Loc. cit.*, p. 219.

[9] "Keating's Cyclopædia of Diseases of Children," Vol. IV., 1890, p. 496.

[10] "Über multiple Herdsklerose des Zentralnervensystems im Kindesalter."—Inaug.-Dissert., Berlin, Oct., 1893.

[11] *Berl. klin. Woch.*, 1887, XXIV., p. 904.

of disseminated sclerosis in adults really date from childhood. One of the youngest cases on record appears to be one published by Dr. Dreschfeld,[1] and this began at 14 months. Pollard[2] has related a case under 2 years, and Jaccoud[3] and Humphreys [4] quote examples in which the initial symptoms started at 2 and 3 years respectively. Gowers[5] thinks, however, that it is exceedingly probable that some cases published as examples of disseminated sclerosis in childhood have really been cases of stationary tubercle of the brain. For the most part, however, disseminated sclerosis is a disease of youth and middle age, as the following tables show:—

ANALYSIS OF MY 33 COLLECTED CASES.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| In | 1 | the disease commenced | between | 5 | and | 10 | years. |
| ,, | 3 | ,, | ,, | 11 | ,, | 15 | ,, |
| ,, | 3 | ,, | ,, | 16 | ,, | 20 | ,, |
| ,, | 12 | ,, | ,, | 21 | ,, | 25 | ,, |
| ,, | 7 | ,, | ,, | 26 | ,, | 30 | ,, |
| ,, | 4 | ,, | ,, | 31 | ,, | 35 | ,, |
| ,, | 2 | ,, | ,, | 36 | ,, | 40 | ,, |
| ,, | 1 | ,, | ,, | 41 | ,, | 45 | ,, |

ANALYSIS OF 60 PUBLISHED CASES.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 8 | cases | began | between | 1 | and | 5 | years. |
| 4 | ,, | ,, | ,, | 6 | ,, | 10 | ,, |
| 2 | ,, | ,, | ,, | 11 | ,, | 15 | ,, |
| 3 | ,, | ,, | ,, | 16 | ,, | 20 | ,, |
| 16 | ,, | ,, | ,, | 21 | ,, | 25 | ,, |
| 15 | ,, | ,, | ,, | 26 | ,, | 30 | ,, |
| 4 | ,, | ,, | ,, | 31 | ,, | 35 | ,, |
| 6 | ,, | ,, | ,, | 36 | ,, | 40 | ,, |
| 1 | case | ,, | ,, | 41 | ,, | 45 | ,, |
| 1 | ,, | ,, | ,, | 46 | ,, | 50 | ,, |

*Race* and *climate* seem to have no special influence in predisposing to disseminated sclerosis.

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[1] *Med. Times and Gaz.*, Feb. 2, 1873, p. 140.

[2] *Lancet*, Aug. 10, 1878, p. 183.

[3] "Traité de Pathologie Interne," 1869, T. I., p. 193.

[4] *Med. Times and Gaz.*, Nov. 3, 1877, p. 491.

[5] *Loc. cit.*, p. 474.

*Social State.*—The disease appears to occur with greater frequency among the poorer classes. Insufficient food and insanitary surroundings are probably the predisposing factors.

*Severe and long-continued hysteria* has been regarded by Mollière[1] as a predisposing cause of disseminated sclerosis. It seems very possible, however, that this authority has confounded cause and effect, as hysterical manifestations are now known to be very common in the early stages of disseminated sclerosis.

*Family Predisposition.*—Consot[2] considers heredity a very constant factor, but other writers are of quite the opposite opinion. According to Ross,[3] its transmission is always indirect, so that unless we can obtain a more full account of the family history than is usually possible, it is easy for us to overlook this cause. Erb[4] gives the case of a young lady whose father also died from disseminated sclerosis. Duchenne[5] also has observed an example of the inherited disease. Leuch[6] publishes a case of a mother and child who both were afflicted with disseminated sclerosis. The mother was suffering from the disease during her pregnancy; the child was healthy until the seventh year, then symptoms of disseminated sclerosis appeared, and the disease terminated fatally. Frerichs[7] and Erb[8] have seen cases of brother and sister suffering from this affection, and Dr. Dreschfeld[9] also has described two remarkably interesting examples in brothers. Pelizæus[10] reports five cases developing in the same family in early life. All the cases were of males, and the ancestral taint had been present in male members of

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[1] *Lyon méd.*, 1875, No. 28.

[2] *Bulletin de l'Académie royale de médecine de Belgique*, Bruxelles, March 14, 1891, S. 4, v., p. 317.

[3] "Diseases of the Nervous System," 1883, Vol. II., p. 755.

[4] *Loc. cit.*, p. 475.

[5] Mentioned in Charcot's "Diseases of the Nervous System," Lecture 8, p. 219.

[6] *Correspondenz-blatt für schweizer Aerzte*, Basel, Jan. 15, 1891.

[7] *Wien. med. Woch.*, 1856.

[8] *Loc. cit.*, p. 475.

[9] *Loc. cit.*

[10] *Archiv für Psychiatrie*, 1885, XVI., p. 698.

the family, passing through the females to their progeny without breaking out in the mothers. Finally, Blomfield[1] relates an undoubted case in a man, the brother of whom, in all probability, is a victim to the same complaint. Hereditary transmission may possibly depend upon some peculiarity of the vascular supply of the central nervous system.

The presence of some ancestral taint other than the disease itself is much more frequently observed. Liegey[2] quotes a family in whom four members suffered from tremor of the hands and lips, the latter interfering with speech. A daughter of one of the members showed typical disseminated sclerosis. The father of one of my cases was stated to have been "paralysed in both legs" for many years. In another, the mother used to have "fits." Another patient had three sisters, two died in convulsions in infancy, and the other is now suffering from chorea; and lastly, the father of another patient was stated to have died in the Prestwich Asylum.

## EXCITING CAUSES.

**The Specific Fevers.**—Considerable attention of late has been directed towards the part that the specific fevers play in the causation of this disease. There is now a generally accepted belief that there is a causative relationship between infectious diseases and disseminated sclerosis. Marie[3] believes that the specific fevers are the most important factors of all in the production of this disease, and it is the opinion of Unger[4] that disseminated sclerosis in children almost invariably follows an infectious disease.

The first symptoms of disseminated sclerosis may develop either in the course of the infectious disease or during convalescence, or more commonly the nervous disease may not manifest itself for several months or years afterwards. In the latter case taken alone the evidence is not conclusive, but when one considers the number of facts of this kind published

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[1] *Brit. Med. Jour.*, Sept. 21, 1889, p. 657.

[2] *Jour. de Méd. de Bruxelles*, 1882.

[3] "Les Maladies de la Moelle," Paris, 1892.

[4] "Ueber multiple inselförmige Sklerose des Centralnervensystems im Kindesalter," Leipzig und Wien, 1887.

by various authors, and the number of cases in which this affection of the nervous system has first shown itself in the course of the infectious disease or during convalescence, it would seem impossible to deny that there exists a relation of cause and effect.

How is it then that infectious diseases attack thousands without nervous sequelæ? It seems to me that there must be in many cases a latent tendency of the nervous system to disease before the influence of the fever poison comes into play. Again, it is probably not the micro-organisms themselves that cause the disseminated sclerosis, but rather toxic bodies manufactured by them; and it may therefore be that in some cases the febrile process is not intense enough for these bodies to be produced in a sufficiently virulent form to cause damage to the nervous system.

The following specific fevers have been frequently noted as antecedents of disseminated sclerosis:—

*Typhoid Fever* seems to be one of the commonest of these. Marie[1] found in 25 cases that disseminated sclerosis followed this fever in 11 instances. Other cases have been observed by Joffroy,[2] Erbstein,[3] and others.

*Scarlet Fever.*—Marie[4] and Totzke[5] mention cases consecutive to this fever. In one of my cases, that of a boy aged eight years, the onset of disseminated sclerosis commenced twenty-two months after an undoubted attack of scarlet fever. Several others gave a history of scarlet fever, but, as there was in each case an interval of several years between the febrile disease and the first signs of disseminated sclerosis, it is doubtful whether any etiological connection existed between the two.

*Influenza.*—Case V. suffered from a severe attack of influenza, shortly before the nervous symptoms commenced. Another case is reported by Massalongo.[6]

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[1] "Les Maladies de la Moelle," Paris, 1892.

[2] *Mémoires de la Société de Biologie*, 1869, p. 146.

[3] *Deutsches Arch. f. klin. Med.*, Bd. X., fasc. 6, p. 596

[4] "Les Maladies de la Moelle," Paris, 1892.

[5] *Loc. cit.*

[6] *Revue Neurologique*, 1893, No. 23, and *Neurologisches Centralblatt*, 1893, No. 10.

*Variola.*—Marie,[1] Westphal,[2] Bourneville,[3] and many others quote examples occurring after smallpox.

*Morbilli.*—Several of my cases had measles in childhood, but here again the lapse of time between the measles and the first nervous symptom was very great. Totzke,[4] Nolda,[5] and others, however, mention cases which quickly succeeded measles. According to Dawson-Williams[6] and several German writers, measles has been repeatedly followed by nervous symptoms very closely simulating disseminated sclerosis (false disseminated sclerosis).

*Pertussis.*—In two of my cases there was a previous history of severe pertussis in childhood. Marie [7] again quotes a case following whooping-cough.

*Diphtheria.*—From a total of **35** cases following fevers, Totzke[8] puts down four cases as resulting from diphtheria. Marie,[9] Moncorvo,[10] and many others quote further examples.

*Typhus* was an immediate antecedent of a case mentioned by Westphal.[11]

*Malaria.*—Torti and Angelini[12] record two cases of chronic malaria in which typical symptoms of disseminated sclerosis developed. Examination of the blood, when the nervous symptoms were present, revealed the malarial parasite. Under treatment, both patients recovered, and the malarial parasite disappeared from the blood. In connection with Torti and Angelini's paper, it is interesting to note a case recorded by Manhiafara[13] of pernicious malaria with bulbar symptoms—paralysis of the facial, hypoglossal, and pneumogastric nerves—in which the vessels in the region of the bulbar nuclei were

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[1] "Les Maladies de la Moelle," Paris, 1892.

[2] *Neue Charité-Annalen*, 1 Jahrg., 1874, S. 427.

[3] Charcot's "Lectures on Diseases of the Nervous System," No. VIII., p. 220.

[4] *Loc. cit.*

[5] *Correspondenz-blatt für schweizer Aerzte*, Basel, November, 1891.

[6] *Brit. Med. Jour.*, December 2, 1893, p. 1213.

[7] "Les Maladies de la Moelle," Paris, 1892.

[8] *Loc. cit.*

[9] "Les Maladies de la Moelle," Paris, 1892.

[10] *Jahrbuch. f. Kinderheilk. u. Psychiat.*, Bd. XXVIII., H. 2, 1888.

[11] *Arch. f. Psych. u. Nerv.*, III., S. 376, 1872.

[12] *Bulletina della Societa Lancisiana degli ospedali di Roma*, 1892, Anno XI.

[13] *Riforma Medica*, 1890.

filled with blood cells containing parasites (parasitic thrombosis). Morton Prince,[1] Camellis,[2] Bignami e Bastianelli,[3] and others, record examples of disseminated sclerosis following malaria, while Boinet and Salebert[4] quote cases of pseudo-sclerosis consecutive to the same disease.

Disseminated sclerosis has also been stated to follow dysentery (Marie) and cholera nostras (Totzke).

**Other Febrile Diseases**—*Acute Rheumatism.*—In Case XIV., definite symptoms of disseminated sclerosis developed soon after an attack of rheumatic fever, though a few slight and indefinite nervous symptoms had been observed previous to the attack. Foxwell[5] reports a case of rheumatic hyperpyrexia (111° F.) with nervous sequelæ simulating disseminated sclerosis.

Cases following erysipelas and acute pneumonia have also been recorded by Marie.[6]

*Unknown Febrile Attacks.*—Many patients give a history of having recently suffered from some febrile attack, about the nature of which they know nothing. In Case IV., the patient was laid up for some time with "slow fever."

**Traumatism.**—The occurrence of a previous injury is mentioned too frequently in the record of cases—about fifteen per cent of all cases reported—for it to be merely a fortuitous circumstance. The principal injuries one finds are falls and blows on the head and spine, concussion of the entire body, and railroad injuries. Two of my cases experienced severe injuries previous to the onset of the disease. The first was a boy, aged eight years, who about the middle of July, 1892, fell off a high wall. He did not become unconscious, but could not rise, and had to be carried home. Severe pain was not complained of, but afterwards it was noticed that the boy could not walk as well as before. He limped with the right foot; this became worse, and in three days after the accident he could not use that leg at all. A month later it was observed that he had a squint, and also that his speech was different to what it used

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[1] *Journ. of Nerv. and Ment. Dis.*, New York, January, 1889.

[2] *Gaz. Hebd. de Méd.*, Août 26, 1887.

[3] *Neurologisches Centralblatt*, 1893.

[4] *Rev. de Méd.*, 1889, Nov. 10.

[5] *Lancet*, May 29, 1886, p. 1012.

[6] "Les Maladies de la Moelle," Paris, 1892.

formerly to be. The boy was admitted into the Manchester Royal Infirmary, as an in-patient, under the care of Dr. Bury, on September 12, 1892, when he presented well-marked signs of disseminated sclerosis. It must be remembered, however, that this boy had scarlet fever about twenty-two months before the accident. My second case was a man on whom a heavy bale fell. He was rendered unconscious for several minutes. Symptoms of disseminated sclerosis began four years afterwards. Such injuries may lead to the slow development of organic changes in the central nervous system, possibly as sequences of slight initial lesions. In the case of the boy mentioned above, it is possible that the morbid process, started by the scarlet fever, was lying dormant until the injury rendered it active.

**Exposure to Cold and Wet.**—Among my cases was a collier whose symptoms immediately followed prolonged exposure to wet and cold. He had occasion to work when down the mine on two consecutive days for twelve hours each day in water which reached up to his waist. After this he was working for a fortnight in mud and water up to his knees; he then noticed that something was wrong with his legs, and very soon he was unable to walk. His legs now improved for a time, but he always had some difficulty in getting about, and soon the characteristic intention tremor appeared in his right hand and arm, then in the left upper extremity, and this was very soon followed by nystagmus and scanning speech. Glynn[1] quotes the case of a man in whom symptoms of disseminated sclerosis followed exposure all night to a temperature of ten degrees below zero, the cold being so intense that his feet were frost-bitten. Baerwinkel[2] also has observed a case in which the patient fell into water and allowed his clothes to dry upon him three days before the first symptoms appeared.

**Exposure to Extreme Heat.**—Lyman[3] relates the case of a man with characteristic signs of disseminated sclerosis, whose first symptom—an apoplectiform attack—immediately followed much exposure to the rays of a tropical sun. Dercum[4] also reports a case following sunstroke.

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[1] *Liverpool Med. Chir. Journ.*, 1887, p. 192.
[2] *Archiv d. Heilk.*, X., S. 590, 1869.
[3] *Medical News*, New York, Nov. 16, 1889.
[4] *Loc. cit.*, p. 122.

**Mental Emotions.**—Prolonged grief was the only discoverable etiological factor in one of my cases, in another there was a history of a severe fright six years before the onset of symptoms. Jordan[1] reports a case of disseminated sclerosis in which the symptoms came on suddenly a few days after a violent mental shock. Spitzka[2] quotes a case, confirmed by autopsy, in which tremor came on immediately after two consecutive frights. Another case following mental shock is related by Focke.[3]

**Syphilis.**—It seems still to be an undecided question whether syphilis plays any part in the causation of disseminated sclerosis. As a rule, a history of syphilis is rarely obtainable. Only one of my 33 cases had undoubtedly suffered from this venereal disease, and in the literature of the subject, syphilis is only very exceptionally assigned as a cause. Again, in the few cases where there has appeared to be a direct causal relationship, the lesion was not typical. There were sclerotic foci, but, in addition, there was a general lesion, particularly of the posterior columns of the cord, and it is to be noted that ependymal and peri-ependymal sclerosis has been more frequently found in the cases of alleged syphilitic origin than those of the typical form. In three cases related by Moncorvo[4] the signs of hereditary syphilis were either observed or matters of history. Two of these improved under mercurials and iodide.

**Pellagra** was succeeded by disseminated sclerosis chiefly affecting the posterior columns of the cord in a case reported by Brigidi-Bandi.[5]

**Pregnancy** has been adduced as an etiological agent by Guérard.[6]

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[1] *Birmingham Med. Rev.*, April, 1892, p. 208.

[2] *Loc. cit.*, p. 884.

[3] Inaugural Dissertation, Berlin.

[4] *Rev. mens. d. mal. de l'enf.*, Paris, 1887, V., p. 241.

[5] *Lo Sperimentale*, December, 1879.

[6] "Essai sur la sclérose en plaques." *Thèse*, Paris, 1869.

## CHAPTER II.

### SYMPTOMATOLOGY OF DISSEMINATED SCLEROSIS.

IN disseminated sclerosis we find a diffused and vague picture, because the disease does not do enough harm in any one part of the brain or spinal cord to destroy entirely its functions; but it teases and weakens various parts of the central nervous system, so that we have a great number of symptoms mixed up together. Considering the irregularity of the sclerotic process, there will be, naturally, considerable diversity as regards the clinical signs in individual cases. The symptomatology varies with the number, size, and distribution of the sclerotic patches. Charcot[1] speaks of disseminated sclerosis as *par excellence* polymorphous. It cannot but strike one as very remarkable that the symptoms should present such a uniform character as is seen in the majority of cases. Moxon[2] endeavoured to explain this uniformity as "a constant average result of the numerous points of disease," but it seems more probable rather that the patches have certain special seats of election, namely, the lateral columns of the cord, the medulla oblongata, and the pons.

I propose to begin my account of the symptomatology by relating Case I., which is a fairly characteristic example of the advanced disease:—

CASE I.—Lewes M., aged 32, weaver, was admitted as an in-patient at the Manchester Royal Infirmary, under the care of Dr. Steell, February 17, 1891.

*Previous History.*—The patient was quite well until 1884, when early in that year he began to be troubled with numbness "just under the knees." This, after lasting a few weeks, disappeared, and he ailed nothing for several months afterwards. In the autumn of 1884, when

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[1] *Loc. cit.*, Lecture VII., p. 184.

[2] *Guy's Hospital Reports*, XX., 1875, p. 437.

climbing a hill, he had to stop on account of weakness and shaking in his legs. He continued his work for another fortnight, but felt very weak and walked very unsteadily. A little later he lost all control over the left leg, and soon after marked tremor appeared in the left arm. In 1885 his speech became affected, and for the last four years he has had pain and difficulty in micturition. Occasionally the urine has dribbled away from him. Two years ago tremor appeared in his right arm. The patient has had no previous illness of importance, and there is no history of injury or syphilis. As far as he knows no relative has suffered from nervous disease.

*Condition on Admission.*—Patient is moderately well nourished and looks fairly intelligent. He is particularly happy, and has a good memory, as evidenced by his long recitations for the entertainment of the other patients. His speech is "scanning." As he lies at rest in bed no tremor is observed, but very marked jerky tremor is noticeable in the arms when any voluntary movement is made by them. Intention tremor is also seen, though in a less marked degree, in the head and lower extremities. No paralysis of the ocular, facial, or tongue muscles. No affection of the muscles supplied by the motor branches of the fifth nerve. No paralysis or wasting of the arms. He is quite unable to stand or walk alone, but with assistance he is able to walk a short distance. In doing so he throws out his legs in an irregular manner, and the gait does not present any spasticity. There is slight rigidity of the legs to passive movement. Both knee-jerks are exaggerated and ankle clonus is obtained on both sides. The wrist and elbow jerks are present on both sides, and the same applies to the plantar reflex. The cremasteric, abdominal, and epigastric reflexes are all absent. A pin is felt and localised, and the point is distinguished from the head all over the body. He complains of "shooting pains" in both legs, but especially in the right; has the girdle sensation, but there is no spinal curvature, tenderness or pain. He can touch the tip of his nose, tell the position of his legs and the direction of passive movements with his eyes closed. There is nystagmus on lateral movements of the eyeballs. The pupils are dilated equally and react normally to light and accommodation. The fundi appear healthy to ophthalmoscopic examination, and hearing, taste, and smell are good. The appetite is bad, and there is occasional regurgitation of fluid through the nose. Incontinence of fæces alternates with constipation. He has pain before and during the act of micturition, and often requires the aid of the catheter. The urine is 1018, acid, and contains phosphates and urates, but no albumen or sugar are present.

February 24.—Had a severe rigor with a temperature of 107·4° F. after catheterisation.

February 28.—The bladder was tapped above the pubis.

March 3.—The supra-pubic tapping was repeated.

March 25.—Paresis of left internal rectus. Urine very ammoniacal, and containing pus and triple phosphates in abundance. Both feet œdematous.

March 28.—Contractures of both legs at knees and hips. Considerable resistance to passive movements at the ankles. The arms are rigid, extended, and applied to the sides of the body. The knee-jerk is very feeble on the right side, absent on the left. Ankle-clonus not obtained on either side; abdominal, epigastric, cremasteric, and plantar reflexes absent. A slight touch with the head of a pin is not felt in the lower extremities, but the point of the pin is readily recognised over the same areas. The legs show marked muscular wasting, and the reaction of degeneration is easily obtained in the tibialis anticus, flexor longus digitorum, peronei, rectus femoris on both sides, and in the left gastrocnemius. No muscular wasting in the arms.

April 17.—A paresis of the right internal rectus has now appeared, but is less marked than that of the left internal rectus.

April 20.—The paresis in both internal recti is now well developed. Both knee-jerks are absent.

April 26.—The patient is much weaker and somewhat drowsy.

April 27.—Death.

The *post-mortem* examination is related in Chapter V.

**Onset.**—The onset of disseminated sclerosis is usually gradual, but may be sudden. In my 33 cases, the invasion was gradual in 31, but abrupt in the remaining two. One of the latter was suddenly seized with weakness in the left leg, while in the other sudden loss of power appeared in the grasp of the right hand. By far the most common mode of onset in children is the sudden or rapid form. When the disease is inaugurated in an insidious fashion, the initial symptoms are usually very obscure, vague, and manifold. The premonitory symptoms may be strictly cerebral in origin, or may be referable to the spinal cord only; they may show themselves in any part of the body. The nature of these symptoms in my 33 cases was as follows:—

SPINAL ONSET.

| | | | | | |
|---|---|---|---|---|---|
| In | 7 | the | first | symptom | was either weakness or stiffness, or inco-ordination of legs. |
| „ | 5 | „ | „ | „ | „ numbness in foot and leg. |
| „ | 4 | „ | „ | „ | „ numbness in fingers and hand. |
| „ | 2 | „ | „ | „ | „ weakness of upper extremity. |
| „ | 1 | „ | „ | „ | „ numbness in hand and side of chest. |

CEREBRAL ONSET.

In 3 the first symptom was tremor of hand.
„ 2 „ „ „ „ headache, associated with vertigo.
„ 2 „ „ „ „ impairment of vision.
„ 1 „ „ „ „ nystagmus.
„ 1 „ „ „ „ diplopia.
„ 1 „ „ „ „ deafness.
„ 1 „ „ „ „ tremor of head and neck.
„ 1 „ „ „ „ headache.

CEREBRO-SPINAL ONSET.

In 1 disseminated sclerosis made its *début* with headache and weakness of a leg.
In 1 dimness of vision, with paresis of a leg, ushered in the disease.

From this table it would appear probable that the disease originates most often in the spinal cord, less commonly in the brain, and much less frequently it commences simultaneously in the brain and cord.

One finds among published cases a few other modes of onset: apoplectiform attacks, in cases by Lyman,[1] Stewart,[2] Lecoq,[3] Bourneville and Guérard,[4] Vulpian,[5] and others; difficulty of deglutition in a case reported by Pepper;[6] herpes zoster in a child under the care of Sparks;[7] Dreschfeld,[8] Humphreys, Pollard,[10] Moncorvo,[11] and others quote cases in children where the onset of the disease was marked by convulsive attacks; gastric crises accompanied by vomiting was the first symptom

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[1] *Loc. cit.*

[2] *Canada Med. Rec.*, Montreal, 1885, XIII., p. 6,

[3] *France méd.*, Paris, 1882, I., p. 398.

[4] "De la sclerose en plaques dissém." Paris, 1869, Obs. XIII., p. 122.

[5] *Memoires de la Société Médicale des Hôpitaux*, 1869, Obs. II.

[6] *International Clinics*, 1894, Vol. I., S. 3, p. 11.

[7] *Med. Times and Gaz.*, Dec. 29, 1877, p. 692.

[8] *Loc. cit.*

[9] *Loc. cit.*

[10] *Loc. cit.*

[11] *União med.*, Rio de Janiero, 1884, IV., p. 49.

in Liouville's[1] case; and psychical derangements, "scanning speech," neuralgic pains, etc., are sometimes primary symptoms of the disease.

From the practical point of view, the early symptoms of the disease are not unfrequently regarded as acts of carelessness, or bad habits. In one of my cases, a barber's assistant, the disease first showed itself in tremor of the right hand, and this was the cause of undue cutting of his customer's chins In another case, that of a domestic servant, the first indication of anything wrong was a repeated dropping of articles of crockery. The left boot of another was unduly worn on the inside of the sole, and lastly, in Case V., an early symptom was irregular marking of numbers on business books.

In a considerable number of my cases the initial symptoms partially or completely disappeared, and the patients remained quite well for not unfrequently considerable periods. But, sooner or later, either a recurrence of these symptoms set in or entirely new troubles appeared in their place. In other cases the numbness or weakness experienced, say in a hand, quite cleared up there, but immediately very similar subjective sensory phenomena, or paretic symptoms, began in the other arm, or in one of the legs.

The order in which the symptoms of disseminated sclerosis appear being so variable I propose to consider them individually, without attempt at chronological arrangement.

**Tremor.**—The most characteristic symptom of disseminated sclerosis is doubtless that tremor on voluntary exertion which Charcot[2] has so admirably pictured in his classical account of the disease. It does not, as a rule, mark the onset of disseminated sclerosis as seen in the preceding table, but in the majority of cases it is present at some stage of the disease. The tremor nearly always makes its first appearance in the upper extremities—in my 33 cases it commenced in the arm in 29 instances. As regards distribution it may affect one limb, or the head and neck alone, but more frequently it is general, though even then it usually varies in degree in

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[1] *Memoires de la Société de Biologie*, Paris, 1870, 5e Serie, Pt. I., p. 107.

[2] *Loc. cit.*, p. 186.

different regions. It has been noticed in the facial muscles by Cohn,[1] and was unilateral in cases by Duckworth[2] and Latham.[3] With the tremor inco-ordination is usually associated, occurring most commonly in the arms, but also often seen in the legs.

When a patient afflicted with disseminated sclerosis lies perfectly at rest in bed, no movements, as a rule, are visible. If quietly seated, with the head unsupported, all that may be noticed is a peculiar nodding of the head, the arms, legs, and trunk remaining still. In some cases the head-tremor is not very apparent, but it may, however, be brought out by getting the patient to throw back his head as far as possible. The tremor is usually most marked in the arms, and its nature is exquisitely demonstrated by the time-honoured test of drinking from a glass of water. On reaching out for the glass oscillatory unsteadiness is noticed, the unsteadiness becomes more marked as he grasps the glass, in carrying the glass to the mouth the oscillations further increase in extent and frequency, getting more and more wild and irregular, and finally becoming very tumultuous as the set task approaches completion—the main direction of the movements is, however, preserved. The most evident movement at first is usually that of flexion and extension at the wrist as the hand is held prone or semiprone, but later in the act the movements, consisting still of flexion and extension, come largely from the elbow and shoulder. This coarse tremor in the arms is also seen well in the acts of picking up a small object, buttoning the coat, sewing, writing, bringing the tips of the forefingers together, or, in fact, attempting any movement requiring a steady hand. The tremor is rendered worse by any attempt to overcome it, by emotion, and under the gaze of bystanders. Some patients attempt to "dodge" the tremor (*i.e.*, to reduce the amplitude of the jerking movements of the head and arm) by throwing the head slightly forwards and fixing it, as it were, between the head and shoulders, and by holding the arm and forearm firmly to the side, but even then their efforts are unsuccessful. The jerky

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[1] *Deutsche med. Woch.*, Leipzig, 1891, XVIII., p. 460.

[2] *Lancet*, 1885, I., p. 879.

[3] *Ibid.*, 1885, II., p. 388.

inco-ordination in the muscles of the legs and trunk may produce unsteady gait. The question of gait, however, will be considered later on. The handwriting of a patient suffering from typical disseminated sclerosis is very characteristic. The

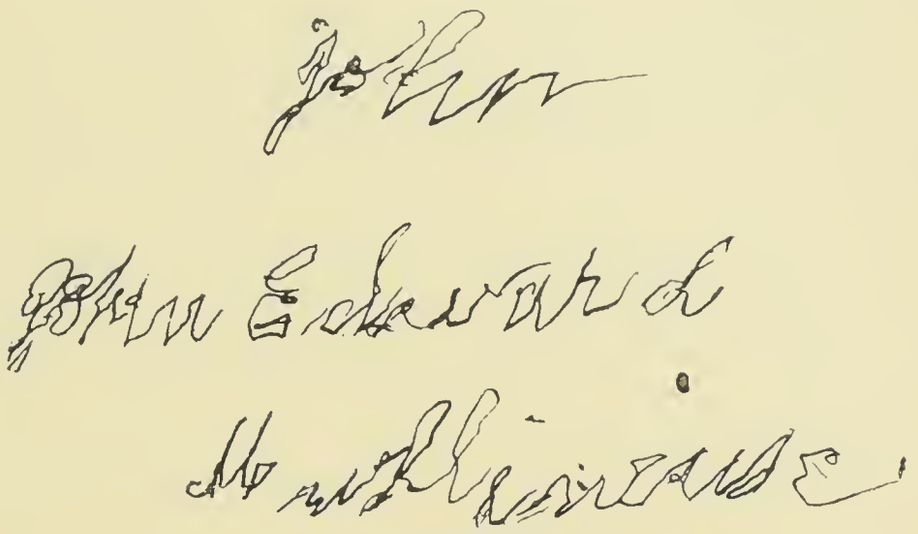

FIG. 1.

Reduced about one-half.

letters are variously distorted, become markedly pointed, and often are disconnected, and the dots and crosses show peculiar irregularity. The following is a specimen obtained from a case in the Crumpsall Workhouse Hospital.

FIG. 2.

Reduced about one-half.

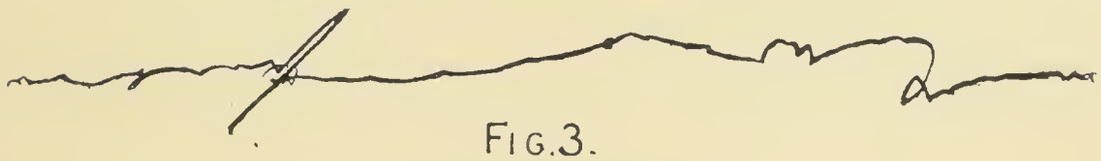

FIG. 3.

Reduced about one-half.

The inco-ordination seen in disseminated sclerosis may be graphically and readily recorded by requesting the patient to attempt to draw a straight line on a sheet of paper. This was done by the same patient whose handwriting has already appeared. Fig. 2 shows the result with the forearm resting upon the table; Fig. 3 the result obtained without such support.

Another method is to ask the patient to hold the pointed end of a pencil in contact with the blackened surface of a glazed sheet of paper fitted on a revolving drum. By means of a tuning-fork of known vibration, to one of the prongs of which a triangular piece of parchment paper is attached, the time can be measured and recorded. The number of oscillations divided by the number of seconds gives the rate of tremor per second. The tracing would first appear as a straight line, but this would rapidly become changed into a zigzag one, the oscillations of which would show increase in size. However, there is some degree both in the extent of the successive vibrations and in the intervals which separate them, though the latter are usually fairly equal. Wolfenden and Williams[1] have shown that the oscillations in disseminated sclerosis are dicrotic to some extent. There is some difference in the results obtained in the estimation of the rate of the tremor in disseminated sclerosis. Thus it has been reckoned at 4—5½ per second by Dutil, 4·6—6·3 by Peterson,[2] 4·6 by Wolfenden and Williams,[3] 7—10 by Charcot, and 6—7 by Gowers.[4] The tremor of disseminated sclerosis diminishes in inverse ratio to the increase of the paralyses and contractures, and in the final stages of the disease, when extensive paralysis has supervened, it not unfrequently disappears altogether.

Is this intention tremor pathognomonic of disseminated sclerosis? Charcot[5] has stated that it occurs in chronic mercurial poisoning, chronic cervical meningitis with sclerosis of the surface of the cord, as well as primary or consecutive sclerosis of the lateral columns. Gowers[6] has seen precisely similar tremor in cases of tubercle of the pons or crus. Gray[7] narrates a case of lepto-meningitis cerebri, in which during life pronounced intention tremor was seen in the upper and lower extremities and tongue, in addition to nystagmus and "scanning speech."

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[1] *Brit. Med. Jour.*, May 19, 1888.

[2] *Journ. of Nerv. and Ment. Dis.*, New York, January, 1889, p. 99.

[3] *Loc. cit.*

[4] *Loc. cit.*, p. 595.

[5] *Loc. cit.*, p. 188.

[6] *Loc. cit.*, p. 474.

[7] *Journ. of Nerv. and Ment. Dis.*, New York, January, 1889, p. 92.

Koenig[1] relates a case in which characteristic intention tremor was present during life; at the autopsy, however, chronic leptomeningitis cerebri, chronic hydrocephalus, and atrophy of the convolutions from sclerosis were found. Erb and Steffen have observed similar tremor in the diffuse form of cerebral sclerosis in children. Again, intention tremor was present in Case II. and Case III., though the former was suffering from a tubercular growth and the latter a cicatrix, both of these pathological conditions being located in the left optic thalamus. Lastly, I have recently had an opportunity of seeing an intention tremor in the right hand and arm of a man afflicted with locomotor ataxia—an out-patient at the Manchester Royal Infirmary under the care of Dr. Bury. On the other hand, tremor has not unfrequently been absent throughout the disease. This was so in Case VI. and Case VII. Tremor never showed itself also, in undoubted examples of the disease quoted by Bastian,[2] Ebstein,[3] Engesser,[4] Erb,[5] Grieff,[6] Jolly,[7] Leube,[8] Ordenstein,[9] Ormerod,[10] and many others. Charcot[11] was of opinion that in many cases which displayed no tremor when they came under observation, this symptom may have existed at an earlier period of the disease. He strongly insisted, therefore, on the value of a careful inquiry into the previous history. Finally, cases of disseminated sclerosis have been related by Schüle,[12] Jolly,[13] and Grieff[14] where the tremor did not cease on rest.

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[1] Read before the Berliner Gesellschaft für Psychiatrie und Nervenkrankheiten, Sitzung von January 10, 1887.

[2] *Loc. cit.*

[3] *Deutsches Arch. f. klin. Med.*, 1872, Bd. X., S. 595.

[4] *Ibid.*, Bd. XVII., S. 557, 1876.

[5] *Loc. cit.*, p. 495.

[6] *Arch. f. Psychiat.*, XIV., p. 287.

[7] *Arch. f. Psychiat. u. Nerv.*, III., S. 711, 1872.

[8] *Deutsches Arch. f. klin. Med.*, Bd. VIII., S. 1, 1870.

[9] "Sur la paralysie agitans et la sclérose en plaques généralisée." *Thèse*, Paris, 1867.

[10] *Bart. Hosp. Rep.*, London, 1888, XXIV., p. 155.

[11] *Loc. cit.*, p. 190.

[12] *Deutsches Arch. f. klin. Med.*, 1871, Bd. VIII., p. 223.

[13] *Loc. cit.*

[14] *Loc. cit.*

In connection with this subject it is interesting to note a case of disseminated sclerosis published by Sinkler,[1] in which an attack of cerebral hæmorrhage arrested the tremor on the hemiplegic side. The tremor continued on the non-paralysed side. This must mean that the lesion inducing hemiplegia also interrupted conduction from the cortex, probably in the internal capsule. Other similar cases have been recorded in which the tremor was renewed as the paralysis disappeared.

*Cause of the Tremor.*—Among the many problems that disseminated sclerosis presents for solution, there are none that have given rise to more discussion than the question of the causation of the tremor. It is a very difficult point to settle, because of the wide extension and multiplicity of the sclerotic patches, and on account of the conflicting clinical and pathological evidence.

Charcot[2] considers it due to the long persistence of the axis-cylinders in the nodules of the sclerosis. Conduction through these may still take place, although when once the medullary sheath is destroyed the conduction will be so retarded that the impulses from the cortex fail to pass in a sufficiently quick succession to cause a continuous contraction. Another view is that there is some specific localisation of the sclerotic nodules. Ordenstein[3] asserts that the tremor depends upon disease of the pons and parts of the brain in front of it. Erb,[4] from an analysis of twenty-two cases of the disease, regards this symptom as the result of the presence of sclerotic patches in the medulla, pons, and crura. Stephan,[5] in a very exhaustive paper, introducing thirty-five cases, comes to the conclusion firstly that the intention tremor is dependent on cerebral localisation of sclerotic patches, and secondly the presence of sclerotic patches in the optic thalami probably causes the tremor. Gray,[6] from a consideration of the fact that intention tremor was observed in two cases of chronic leptomeningitis cerebri, thinks that this

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[1] *Journ. of Nerv. and Ment. Sci.*, New York, Vol. XV., New Series, 1890.

[2] *Loc. cit.*

[3] *Loc. cit.*

[4] *Loc. cit.*, p. 495.

[5] *Archiv f. Psychiatrie*, Bd. XVIII., S. 734, and Bd. XIX., S. 18.

[6] *Loc. cit.*

phenomenon is due to lesion of the cerebral cortex, or of the underlying white strands. Unger[1] is much of the same opinion, and Pasternatsky[2] dogmatically states that the extreme muscular oscillation seen in advanced cases is due to irritation of the cortical motor fields.

Before venturing to express an opinion on the subject, I propose first to relate several cases of other diseases exhibiting exactly similar tremor as that found in disseminated sclerosis.

Case II.—Albert M., aged six years, was admitted as a home-patient at the Chorlton-upon-Medlock Dispensary, under my own care, on December 17, 1894.

The patient was apparently quite well until seven weeks ago, when the mother noticed that he dragged his left leg on walking. Two or three days after this it was observed, when he was taking his food, that he held the spoon in his left hand, and, when his mother made him use the right hand for that purpose, this latter hand began to tremble. At first the trembling was slight, but it gradually got more and more marked. For the last three weeks he has complained of severe frontal headache, and there has been vomiting for the last four days. Lately, also, he has not seemed to see things well.

The father died two years ago from "apoplexy." The mother gives a history of four miscarriages out of eight pregnancies, and has had a sore throat for six months at a time. The mother's father died from "consumption."

*Condition on Admission.*—An exceedingly well-marked coarse jerky tremor is seen in the right arm on movement. This disappears entirely when the arm is at rest. The movements come largely from the shoulder. There is no nystagmus or syllabic speech. The right arm and leg are distinctly weaker than those of the left. No facial paralysis. The right knee-jerk is exaggerated, the left normal. There is well-marked and persistent ankle-clonus on the right side, but ankle-clonus is not obtained on the left. Both wrist-jerks are present and about equal on the two sides; the epigastric, abdominal, cremasteric and plantar reflexes are all obtained, but show no difference on the two sides. There is marked rigidity noticed on passive movement of the right knee-joint. The patient has difficulty in standing unsupported, but shutting of the eyes makes no difference, and there is no particular reeling in one or other direction. With assistance he is able to walk,

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[1] *Loc. cit.*

[2] *Jahrbücher für Psychiatrie*, III., 3, 1882.

and the gait is distinctly ataxic. Sensation is normal everywhere. The bladder and rectal functions are normal. There are no signs of congenital syphilis, and the lungs appear quite healthy.

December 19.—The vomiting has quite ceased under bismuth, but treatment has in no way influenced the headache.

December 22.—Well-marked optic neuritis of the left eye. There appears also to be inflammation of the right nerve, but of this I cannot be quite certain, as conjunctivitis, with a slightly cloudy cornea, was present on the right side, and the concomitant blepharospasm also rendered ophthalmoscopic examination exceedingly difficult. The other cranial nerves appear to be normal. Towards the close of the somewhat prolonged ophthalmoscopic examination, the patient was suddenly seized with an attack of tetanoid rigidity. He became unconscious, the head was bent back, the spine arched and the whole body became extremely rigid, the teeth were clenched, and both eyes were turned to the left. The face preserved its natural colour. This condition was kept up for about three minutes, and then the muscles gradually relaxed, and there was a return to complete consciousness. This tonic condition was not succeeded by any clonic contractions. The mother now tells me that he had three similar attacks during the preceding night. I put my patient to-day on large doses of iodide of potassium, combined with mercurial inunctions.

December 25.—Has had three attacks of tetanoid rigidity between six and eight this morning, the last one being the severest yet experienced. He falls asleep, worn out, after each attack. When awake he is constantly moaning and complaining of his head.

December 24.—Had five attacks of tetanoid rigidity early this morning. They followed rapidly upon one another. The intention tremor is not quite so marked as when first seen, and the grasp of the right hand is weaker.

December 25.—No control over bladder or rectum. Death at 11 p.m.

*Autopsy* on December 26, sixteen hours after death. *Post-mortem* rigidity very marked. Extensive dorsal hypostasis.

I could only obtain permission to examine the brain. Skull-cap normal. Membranes congested, but not showing any signs of inflammation. A distinct firm tumour could be felt in the left side of the brain. On opening the left lateral ventricle in the usual way, a very considerable quantity of clear serous fluid gushed out. No excess of fluid in the right lateral ventricle. The tumour was found to be situated in the left optic thalamus. Its relative size, position, and relations are seen in Figs. 4 and 5. On microscopical examination it proved to be tubercular.

Case III.—Henry W., 47, was admitted as an in-patient at the Manchester Royal Infirmary, under the care of Dr. Harris, on August 9, 1889. The patient stated that the tremor of the right arm began fourteen years ago.

*Condition of the nervous system on admission.*—As he lies in bed no tremor is present, but if he is told to hold out his right hand, violent tremors occur, more marked if his attention is directed to the arm. The tremor consists of violent jerky movements at the elbow and shoulder, namely flexion and extension. There is no loss of power of the right arm. No tremor in the other limbs. He also shows hemianæsthesia, which, however, varies from time to time.

He died from phthisis on November 25.

At the *autopsy* on November 28, a little behind the centre of the left optic thalamus was a firm bluish-white cicatrix one-third of an inch in diameter. Posteriorly the cicatrix was a quarter of an inch from the white matter of the cortex, anteriorly an eighth of an inch ; from above downwards it occupied the centre of the left optic thalamus. The rest of the nervous system was normal.

It will be seen that in both these cases there was very marked intention tremor in the right upper limb. Case II. had, in addition, slight but distinct paresis of the right arm and leg, whereas in Case III. there was no such weakness, but the latter displayed at times hemianæsthesia on the right side. I found at the post-mortem examination on Case II. a tubercular growth about the size of a walnut occupying the left optic thalamus (Fig. 4).

A vertico-transverse section through the tumour showed that the growth was pressing on the left internal capsule (Fig. 5).

At the autopsy on Case III. a large and firm cicatrix was discovered in the left optic thalamus, and here, again, there could be little doubt that the internal capsule was compressed by the cicatricial and enlarged optic thalamus.

Gowers[1] relates the case of a child in which the first symptom was jerky inco-ordination of the right arm, exactly like that of disseminated sclerosis, followed by palsy of the arm, then of the leg and face, then of the left third nerve, and later, of the right

[1] *Loc. cit.*, p. 474.

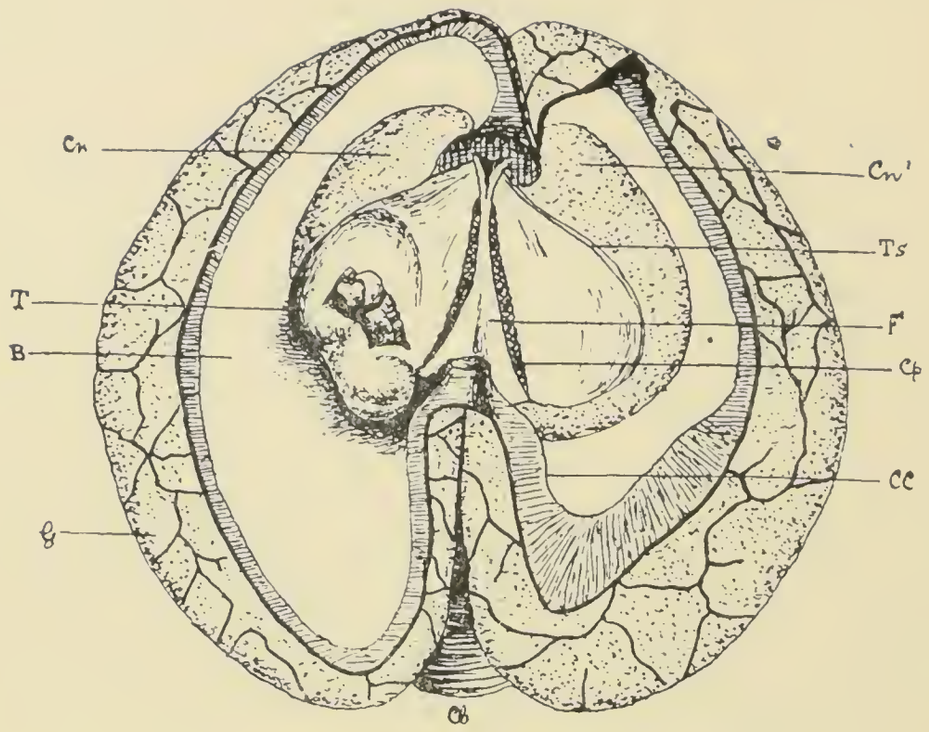


FIG 4

CASE II.—Both lateral ventricles have been partially opened out, displaying—T, a tumour in the left optic thalamus; B, body of left lateral ventricle; CN, left caudate nucleus; CN1, right caudate nucleus; F, fornix; CP. choroid plexuses; Ts, taenia semicircularis; Cc, corpus callosum; G, cortical grey matter; and CB, cerebellum. One-third natural size.

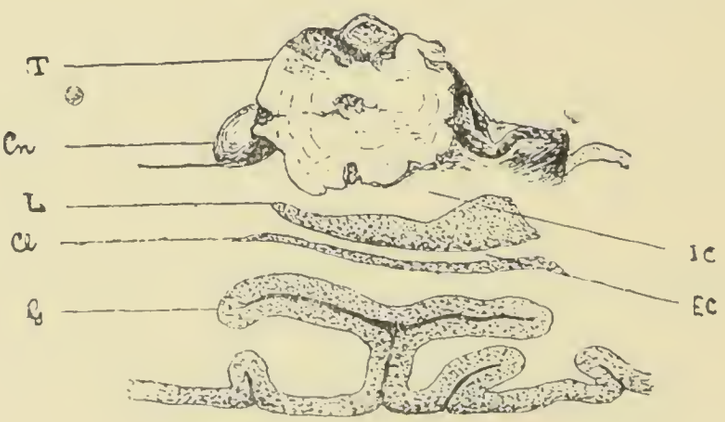


FIG.5.

CASE II.—Vertico-transverse section through the growth and left cerebral hemisphere. T, tumour; Ic, internal capsule; Ec, external capsule; L, lenticular nucleus; CL, claustrum; CN, caudate nucleus; G, cortical grey matter. Natural size.

also. After death a tubercular growth was found in the left crus cerebri. Gowers[1] has also met with this symptom in a case of tubercle of the pons.

The reason that intention-tremor is not always noted when intra-cranial growths press upon the motor tracts is that, perhaps, in these cases the tumour grows so rapidly that the nerve tubules are quickly destroyed, and not slowly and gradually pressed upon and obliterated by degrees. The tremor in all cases, if the patient lives, sooner or later gives way to paralysis, so that if the stage of tremor be short, it may not be observed.

A tumour slightly compressing the motor paths would implicate some nerve fibres more than others, destroying entirely the functions of a few, diminishing the conducting power of a considerable number, and allowing others to escape entirely. It seems to me that the sclerotic patches act in a precisely similar manner. In the centre of a patch some of the tubules are entirely gone; as we get nearer the periphery we find the axis-cylinders more or less bared of their myeline, and in the peripheral zone some fibres remain intact. The analogy can be carried further; thus, the tumour may advance until the nerve tubules are completely destroyed, so in the late stage of the sclerotic disease the tremor likewise disappears.

It is a fact well known to physiologists that a certain number of motor impulses per second are required to keep a muscle steadily contracted. It is evident, therefore, that if the stimuli proceeding from the muscle to the cortex should, on account of interference with conduction by either a slightly pressing tumour or a sclerotic patch, be too few, tremor, and not steady contraction of the muscle will occur. Again, the physiologists tell us that in all co-ordinated movements a number of muscles, the actions of which are antagonistic to one another, are brought into play, and it is by the proper antagonistic actions that the performance of delicate movements becomes possible. In both tumour and sclerotic patch, as previously stated, the nerve fibres are unequally implicated. Unless the amount of contraction of each of the antagonistic muscles is exactly graduated, the balance will be disturbed, and there will be a tendency to oscillatory movement. As the amount of contraction in each muscle, or

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[1] *Loc. cit.*, p. 511.

group of muscles, is regulated by the stimuli sent down to it from the cortical nerve centres, it is evident that if the nerve tubules from the motor cells be affected more than those which supply the antagonistic or regulating muscles, inco-ordination, as well as tremor, will occur.

To my mind, any particular localisation of the disease is unnecessary, provided only that the spot be anywhere in the motor paths, between the cerebral cortex and the cervical enlargement of the cord, as below the latter the arms could not be affected. Lesions of the lower cervical, dorsal, and lumbar regions of the cord seem never to produce tremor in the muscles below. We get no intention tremor in simple chronic myelitis, even when there are several foci, and, again, tremor was absent when the sclerotic patches were limited to the cord, in cases by Ebstein,[1] Engesser,[2] Vulpian,[3] and others. I cannot find among the literature of the subject any case of the disease entirely confined to the cord, and yet presenting intention tremor. Again, in Kelp's[4] case, and in the other rare instances where the disease was purely cerebral, intention tremor was present. However, as a matter of fact, resistance to conduction is most often met with in the pons, medulla or crura.

Stephan's[5] view cannot be the correct one, for Case I. and Case IV. are strong opponents to it; they both presented very marked intention tremor, and yet no trace of sclerosis could be found in either optic thalamus. Again, in Case VI., the sclerotic patches were small and trivial above the cervical enlargement until both optic thalami were reached, and there several larger foci were discovered. According to Stephan, we ought, undoubtedly, in this case to have had tremor, as in some of his cases the sclerosis of the optic thalamus was very slight. In those cases where leptomeningitis of the brain caused intention tremor, the meningeal inflammation was an irritative lesion, which possibly interfered with the initiation of impulses.

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[1] *Loc. cit.*

[2] *Loc. cit.*

[3] *L'Union méd.*, 1866, No. 67.

[4] *Deutsch. Archiv f. klin. Med.*, X., S. 224, 1872.

[5] *Loc. cit.*

**Paresis and Paralysis.**—Besides tremor, other motor disorders are very frequent in disseminated sclerosis. Some amount of paresis in the extremities is one of the commonest and earliest symptoms of the disease. This loss of power very often begins in one leg, then invades its fellow or one of the arms, but no prediction as to the order in which the various muscular groups will be attacked can safely be made. Weakness has occasionally commenced in both legs at the same time, and in a few cases the paresis has shown itself first in the upper extremities. That the latter is unusual is seen from published cases, and by the fact that, in only one of my 33 cases of disseminated sclerosis, the first sign of loss of power was some weakness in the grasp of the left hand.

It seems to me very remarkable and exceedingly difficult of explanation that paresis should nearly always begin first in the legs, while on the other hand, that tremor should be first evident in the arms. Again, almost without exception, tremor remains more pronounced in the arms, whereas the lower extremities usually exhibit paralysis in a more marked degree.

Not unfrequently, paresis, after making its appearance in a limb, passes off for a time, then nearly always returns more marked than ever, the other limbs having perhaps been attacked in the meantime. Buzzard[1] does not think that there is any disease of the spinal cord, except disseminated sclerosis, in which there is found this kind of recurrence of loss of power after an interval of partial or complete recovery, and he considers it one of the most characteristic features of the disease. A similar condition is, however, not unfrequently seen in syphilitic disease of the nervous system. To my mind, the most probable explanation of this apparent recovery, followed by a return of the weakness, is, that in the incipient sclerotic process, an inflammatory exudation takes place around the vessels (see Chapter V.) This exudation irritates and presses upon the nerve tubules, and in this way causes the loss of power. Soon a shrinkage in this exudation takes place, the pressure ceases, and the persistence of the axis-cylinders admits of a perfectly functional recovery. The process may, however,

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[1] *Lancet*, Jan. 12, 1895, p. 79.

after a time, become active again, and proceed to such an extent that well-marked permanent paralysis now appears in place of the early transitory loss of power. In those cases where the loss of power disappears permanently, it may be that the sclerotic process remains quiescent at the stage allowing of possible recovery.

Oppenheim[1] claims to have found a new symptom "in a rapid exhaustion of muscular power in non-paralysed parts—viz., a first movement being made with full power, a second with less, and so on to complete inertia."

**Spasticity of Muscles.**—As the muscular weakness comes on it is usually accompanied by an excess of myotatic irritability which goes on to spasm. The spasm, like the paralysis, is usually most marked in the lower limbs, and is probably due to implication of the lateral columns of the cord.

**Gait.**—According to Oppenheim[2] the following varieties of gait are met with in disseminated sclerosis: (*a*) The most frequent is the well-known *spastic-paretic* gait. (*b*) A pure *ataxic* gait. This is very rare, and is similar to the gait seen in locomotor ataxia. (*c*) A *spastic-paretic-ataxic* gait, which Oppenheim says is very frequently met with. In this form the patient walks slowly with the legs stiff, the feet apart, the point of the foot scrapes the ground, and when the foot is once lifted from the floor, the leg is sharply raised and the heel is brought down in a stamping manner. The gait exhibits weakness, ataxia, and the spastic condition. (*d*) A *vertiginous* gait, which is a disturbance of walking produced by giddiness; the patient staggers like a drunken person. (*e*) A combination of all the four forms put together, constituting a *spastic-paretic-ataxic-vertiginous* gait. This is not very common. (*f*) A *tottering* gait. Though the muscular power of the legs is very good, the patient is not able to walk on account of marked tremor of the head and oscillations of the body.

Various combinations of the above are met with, and sometimes their character undergoes considerable changes in a short time.

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[1] *Berlin. klin. Woch.*, 1887, XXIV., p. 904.

[2] *Charité-Annalen*, 1889, p. 413.

The majority of my 33 cases of disseminated sclerosis showed the gait of spastic paraplegia; in six cases, however, ataxia was a very prominent feature; in another, the gait was "reeling" and very like that seen in cerebellar disease; and, lastly, the walking in one case closely simulated that of a tabetic patient.

**Rigidity and Contracture.**—Sooner or later, in the course of the paretic symptoms, the lower limbs, either spontaneously or under excitement, become stiffened. At first the rigidity is transitory, of short duration, and there are long intervals between the attacks. One of Moxon's[1] patients used to sit in an elbow-chair, in order that when stiffening attacked the legs she could hold on to the arms of the chair and save herself falling down to the floor. Later, however, the rigidity becomes permanent. In my 33 cases of disseminated sclerosis rigidity was noticed in 12 instances; in seven it was slight and in the legs; in three the lower extremities were stiffly extended, the thighs on the trunk, the legs on the thighs, and the feet on the legs, and these limbs lay in close apposition and could only be separated with difficulty, while the arms were uninvolved; in the remaining two—Case I. and Case IV.—the flexor contractures had taken the place of the extensor rigidity in the legs, bending every joint, while the arms were rigid and applied to the sides of the body. The flexor contractures were productive of considerable pain and disturbed the patient's sleep. Case IV. used to bitterly complain of very painful muscular twitchings in the contracted limbs. On the other hand, the extensor rigidity caused little or no actual pain. The upper extremities are rarely the seat of contractures, but are sometimes when the paralysis has extended to the arms. Contractures commenced in the hands of Case IV. shortly before death. Schüle[2] observed in one case a temporary cataleptic or tetanic rigidity of the muscles of the upper extremities. Rigidity and contracture occur in direct proportion to the paralysis. In the stiffened limbs violent tremblings are apt to occur either spontaneously or under irritation, such as a draught of cold air, the prick of a pin, the electric current, tickling, and the like. They may last several minutes, frequently recur, and may

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[1] *Loc. cit.*

[2] *Deutsches Archiv f. klin. Med.*, 1871, Bd. VII., p. 259.

extend from one limb to its fellow, or even affect the whole body. These attacks of tremor were observed in Case XIV., where they could be arrested by flexing the big toes.

**Muscular Sensibility.**—As a rule the muscular sense is unaffected. None of my cases, even the most advanced, showed any loss of muscular sensibility. Engesser,[1] however, has published a case in which there was considerable impairment of the muscular sense with much staggering when the eyes were closed.

**Reflex Actions.**—The reflexes are somewhat variable, and in very young children are often difficult to determine. The deep reflexes, especially in the lower extremities, are usually exaggerated. An analysis of the deep reflexes in my 33 cases is as follows :—

| Knee-jerk. | | Ankle-clonus. | |
|---|---|---|---|
| Increased | 17 | Present | 15 |
| Much increased | 7 | Absent | 7 |
| Tremendously exaggerated | 3 | Excessive | 5 |
| Lost | 1 | Obtained occasionally | 3 |
| Normal | 4 | Present one side. Absent on other | 3 |
| Absent on one side. Increased on other side | 1 | | |

| Wrist-jerk. | | Elbow-jerk. | |
|---|---|---|---|
| Present | 5 | Present | 6 |
| Absent | 6 | Absent | 7 |
| One side very feebly. Other side absent | 2 | Not tried for | 20 |
| Not tried for | 20 | | |

The jaw-jerk was only tried for in one case, and was then elicited. In several cases which showed increased knee-jerk and ankle-clonus in their earlier stages, these reflexes disappeared when the cases became very advanced.

In the case of a boy aged eight years, an in-patient at the Manchester Royal Infirmary, under the care of Dr. Bury, in 1892, there was seen absence of the knee-jerk on one side, with an increased knee-jerk on the other, while ankle-clonus was obtained on both sides. This condition, which at first sight appears somewhat paradoxical, is easily explained according to Buzzard[2] — who showed another such case before the Harveian

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[1] *Loc. cit.*

[2] *Lancet*, Jan. 28, 1888.

Society—by remembering that a patch of sclerosis occurring in the lumbar enlargement of the cord, at the appropriate level, would necessarily, if it involved the anterior grey matter, destroy the reflex, while at the same time the patches involving the antero-lateral columns would give rise to ankle-clonus, which is dependent upon the functioning of a lower segment of the cord. On the other side of the cord there are probably no patches in the lumbar enlargement involving the reflex arc, but there is disease higher up on that side which would allow of an increased knee-jerk and ankle-clonus on that side.

In a case of disseminated sclerosis, at the Crumpsall Workhouse Hospital, contractious of the gastrocnemius were very easily set up, quite spontaneously, when the patient was seated in a chair, simply by making him raise his heel from the floor. The patient had considerable difficulty in arresting this clonus when once it was started. I have recorded it in a graphic manner by using the following device. My materials were a

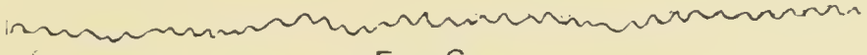

FIG. 6.

Reduced about one-half.

sheet of ordinary writing paper, a copying-ink pencil, and my watch. By placing the paper on the knee of the leg exhibiting this clonus, a distinct oscillatory movement was imparted to the paper. Then by drawing the paper steadily across the knee with my left hand, and holding at the same time, with the other hand, my pencil somewhat loosely against the paper, but keeping the pencil at a spot about the middle of the knee, I obtained a series of very regular oscillations on the paper, Simultaneously I noted with my watch the time taken in drawing the paper across the knee. I took twenty such tracings, and in each I counted the oscillations and divided them by the number of seconds. The mean of these calculations resulted in about six contractions per second. Fig. 6 shows a tracing of these movements, which are quite different from the wild oscillations seen in the tremor of disseminated sclerosis.

Westphal's paradoxical muscular phenomenon is sometimes observed in disseminated sclerosis, and a very exaggerated, intense, and persistent variety of ankle-clonus is occasionally

seen in the so-called "spinal epilepsy" of Charcot and Brown-Séquard. On passive dorsal flexion of the foot a very wild form of clonic tremor may occur first in the calf muscles, then may spread up the thigh to the other leg, and may finally set up general tremor. In two of my cases—Case XIV. and a workhouse patient—this phenomenon was obtained, but here it did not become general, but confined itself to the lower extremities. The method suggested by Brown-Séquard of arresting this "spinal epilepsy," by forcible flexion of the great toes, was tried with perfect success in Case XIV. "Spinal epilepsy" was observed in the case of a child published by Dr. Dreschfeld.[1] According to Westphal[2] this very exaggerated ankle-clonus is never seen in locomotor ataxia.

The superficial reflexes behaved as follows in the cases where they were tested:—

| | Present. | | Very lively. | | Absent. | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Plantar ..... | 15 | ... | 10 | ... | 3 | In 2 present on one side, absent on the other. | | | | |
| Abdominal..... | 16 | ... | 6 | ... | 4 | „ 1 | „ | „ | „ | „ |
| Epigrastic..... | 15 | ... | 5 | ... | 5 | „ 1 | „ | „ | very feeble | „ |
| Cremasteric ... | 9 | ... | 3 | ... | 2 | „ 1 | „ | „ | absent | „ |

The gluteal, interscapular, conjunctival, and other superficial reflexes were not examined for. Buzzard[3] attaches considerable diagnostic importance to the plantar reflex, which he considers to be very rarely absent in disseminated sclerosis. On the other hand, he says, absence of plantar reflex is the rule in hysterical paraplegia. The left plantar was the only reflex obtainable in the final stages of Case IV., while in Case I. every reflex had disappeared a month before death, except the right knee-jerk.

**Sensory Symptoms.**—A very considerable number of my cases complained some time in the course of the disease of slight subjective sensory disturbances, such as numbness, tingling, formication, and neuralgic pains in different parts of the body. Disseminated sclerosis is often ushered in by one of these. On the other hand, when one comes to test the sensory apparatus,

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[1] *Loc. cit.*

[2] *Berlin. klin. Woch.*, No. 1, 1878.

[3] "Simulation of Hysteria by Organic Disease," London, 1891, p. 98

it is nearly always found to be normal as far as tactile, painful, and temperature impressions are concerned. If, however, the disease is very advanced, and there is diffuse sclerosis of the cord, one may find very extensive sensory alterations. Thus, in Case IV., in the legs and abdomen, sensation for touch was considerably affected; in addition, there was analgesia, also considerable impairment of the temperature sense, polyæsthesia was noticed in the left leg, and lastly allochiria was present—a touch on the right leg was referred to the left, and *vice versâ*. The anæsthesia and analgesia in this case, however, were never complete, and were situated in patches. Case IV. also used to complain of a feeling "as if cold water was continually running down his legs." In three other cases there were several patches of anæsthesia in the legs, which developed somewhat suddenly and were very variable. According to Oppenheim[1] this acute development and transitory character of the anæsthesia is pathognomonic of disseminated sclerosis. The analgesia of syringo-myelia may have some resemblance to it, inasmuch as it also may occupy exclusively zones of skin and mucous membrane. The scarcity of sensory symptoms in disseminated sclerosis is, at first sight, somewhat surprising; but it is a well-known fact that in the sensory nerves a lesion, which permanently interrupts motor conduction, may scarcely affect sensory conduction, and in other cases of compression of the various components of the spinal cord the same escape of sensory conduction is often observed. But absence of marked sensory symptoms is not characteristic of disseminated sclerosis. Berlin[2] found in 15 out of 39 cases that there was marked affection of the sensibility. In Engesser's[3] case there was very considerable and extensive diminution of the cutaneous sensibility. Lightning pains were present in several of Bourneville's[4] cases, and a case published by Zenker[5] had repeated gastric crises. Case I. experienced the girdle sensation, complained of shooting pains in the legs, and showed some diminution of

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[1] *Berlin. klin. Woch.*, 1887, p. 904.

[2] *Deutschcs Archiv f. klin. Mcd.*, XIV., S. 103, 1874.

[3] *Loc. cit.*

[4] "De la sclérose en plaques dissém.," Paris, 1869.

[5] *Zeitschrift für Mcdizin*, Band III., Reihe, 1865, p. 228.

tactile sensibility in the lower extremities. After death the posterior columns were found largely involved (Figs. 29, 30, and 31), and this readily accounted for the above symptoms. Hemianæsthesia is said very occasionally to occur, and to be caused by the development of a sclerotic nodule in the sensory path within the brain. In children, like adults, sensibility often continues normal throughout the course of the affection, but in cases by Drs. Dreschfeld[1] and Pollard[2] there was slight diminution of sensibility in the lower limbs. In Schüle's[3] case there was noted at one time a general anæsthesia, which, however, was only temporary. The following case is especially interesting on account of the presence of marked sensory disturbances.

Case IV.—Josiah C., aged 25 years, blacksmith, unmarried, was admitted as an in-patient at the Manchester Royal Infirmary, under the care of Dr. Dreschfeld, on May 6, 1893.

*Family History.*—Unimportant.

*Previous History.*—As a child, patient had measles and a "slow fever," of the nature of which he can tell nothing, except that he was very ill, and kept his bed for a long period. Since childhood his health has been good. No history of alcoholism, rheumatism, or syphilis.

*History of Present Illness.*—About four-and-a-half years ago the patient noticed that the sight of his right eye became dim. This gradually became worse until vision with that eye was very imperfect, then it began slowly to improve. Six months later he found that his left leg dragged on walking, and that his speech had become affected. Two years ago he began to have very considerable difficulty in walking, and was unable to get along without assistance. During the last twelve months he has been chiefly confined to bed.

*Condition on Admission.*—The patient presents the appearance of a fairly-nourished, healthy man. He is moderately intelligent, neither very depressed nor very cheerful, and has rather a sleepy look. On voluntary effort there are tremors in both arms. The movements of the arms are good, but the patient has difficulty in touching the tip of his nose with a given finger. The wrist- and elbow-jerks are just present on both sides. There is marked rigidity of the left leg to passive move-

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[1] *Loc. cit.*

[2] *Loc. cit.*

[3] *Loc. cit.*

ment, but in the right leg the rigidity is slight. The leg is kept semi-flexed. In both legs, from the hips to the ankles, there is partial analgesia and anæsthesia; above Poupart's ligament there is normal sensation to heat and cold, painful and tactile impressions. Both knee-jerks are present, but no ankle-clonus can be obtained on either side. All the superficial cutaneous reflexes are absent, with the exception of those of the soles. The patient smells camphor quite well with either nostril. Left eye $V = \frac{6}{60}$; right eye, $V = \frac{3}{60}$. In both there is optic atrophy, the discs being pale and the vessels small. No signs of optic neuritis are to be seen. Marked nystagmus of both eyes, but all the movements of the eyeballs are performed well. The pupils react directly and indirectly to light, and accommodate readily for near and distant objects. There is a discharge from the right ear, which has been going on ever since he had measles in childhood. On that side he can only hear the tick of a watch at a maximum distance of three inches. No discharge from the left ear, and a watch can be heard on this side at a maximum distance of 18 inches. Taste normal. No affection of the muscular branches of the fifth nerve. No facial or lingual paralysis. Movements of soft palate good, movements of sterno-mastoids normal. Circulatory and respiratory systems normal. The tongue is a little furred, and the bowels are usually confined. There is involuntary passage of urine, but no dribbling; the bladder seems to fill to a certain point, and then there is a sudden emptying. The urine is normal.

May 15.—Complete anæsthesia over the peroneal muscles in both legs.

May 19.—Urine and fæces passed involuntarily. There is slight pain during the passage of the urine, and the latter is alkaline, and contains pus and mucus.

May 23.—Severe aching pain in both hip- and knee-joints. Several very marked patches of anæsthesia and analgesia in the left lower extremities. The temperature sense is greatly impaired in certain parts of the legs; hot bodies are declared to be cold, though cold bodies are usually correctly described. There is increased deposit of pus in the urine.

June 14.—The knee-jerks show a tendency to disappear. The upper limit of the anæsthæsia is marked on both sides by a line running from the anterior superior iliac spine upwards and inwards obliquely across the abdomen.

June 19.—Both knee-jerks are absent. There is complete incontinence of fæces.

The patient's condition remained much the same during July and August.

September 15.—Marked weakness of both arms. He cannot move his legs at all, and these limbs are stiffly flexed at the knees and hips. He complains of very severe painful "twitchings" in the lower extremities, and these keep him awake at night. Sensation to touch has not absolutely disappeared in the legs, though it is considerably impaired, especially in parts; also analgesia, though well-marked, is not complete. Localisation of tactile and painful impressions is, however, very faulty. A touch or prick on the inside of the great toe is referred to the inside of the shin; a touch or prick on the leg to the thigh; one on the thigh to the leg. Sometimes, the impression is referred to the opposite limb, and occasionally in the left leg one prick is thought to be several. At certain parts of the lower limbs the patient cannot discriminate at all between hot and cold bodies. All the reflexes have disappeared excepting both plantar. The muscles of the lower extremities are not atrophied. Bedsores have formed over the right and left heels, buttocks, and left great trochanter.

September 17.—There is a commencing bedsore over the external condyle of the right femur. He complains that his "legs feel as if cold water were constantly running down them."

September 18.—Slight anæsthesia, but more marked analgesia over the right half of the abdomen. In the upper extremities sensation is normal, but there is very marked rigidity of the arms to passive movements. They lie fully extended, and in close apposition to the sides of the body. The sight is much worse, and the speech is very unintelligible. Nystagmus, though still marked, is less than it was. Absolute loss of control over the bladder and rectum.

October 28.—Condition much the same. He still complains bitterly of the painful "twitchings" in his legs.

November 6.—Contractures are developing in the hands.

November 30.—The right plantar reflex has disappeared, but the left still persists.

December 13.—Commencing diarrhœa.

December 20.—Diarrhœa very considerable.

December 27.—Death.

The *post-mortem* examination is related in Chapter V.

**Ocular Symptoms.**—Eye symptoms are frequently met with, and are important features of the disease. Disturbances take place chiefly in the external ocular muscles, in the iris, and in the optic nerve.

*The Extrinsic Muscles of the Eyeball.*—The most frequent eye symptom in disseminated sclerosis is *nystagmus*. According

to Charcot[1] it occurs in half the total cases, and this is confirmed by Pritchard,[2] who found nystagmus in 50 per cent of collected cases, and by Marie,[3] who noted nystagmus in 7 out of 14 examples of the disease in children. Nystagmus was present in 29 out of my 33 cases of disseminated sclerosis. In one of these cases nystagmus was the first sign of the disease, and in another it was the second symptom noted; in the case of a woman attending Hammond's[4] Clinic nystagmus was the only symptom for over a year, and then gradually other phenomena of disseminated sclerosis made their appearance. The nystagmus differs somewhat from the ceaseless oscillations with which ophthalmic surgeons are familiar by it being necessary, as a rule, to put first the ocular muscles on the stretch. Occasionally, however, nystagmus is constantly present. It is most commonly best brought out by movements in the lateral direction, then in the upward direction, and least often on looking downwards. Rotatory nystagmus is rare, so also is lateral nystagmus on movement in one direction rotatory on movement in another. Monocular nystagmus is said to be occasionally met with, and a case showing vertical nystagmus has been published by Bouchard.[5]

The cause of the nystagmus of disseminated sclerosis is obscure. It has been thought by some to be analogous to the volitional tremor. The movements of nystagmus, however, are much more regular, more frequent, and usually appear earlier than the intention tremor. Again the constancy of the nystagmus makes it very unlikely that a patch of sclerosis always develops in the path for the ocular movements. Perinaud[6] considers that nystagmus is a paretic tremor, depending upon central nervous incompetence, and quotes in support of this a case under the care of Raymond, in which the paralysis was complete for the movement of the eyes to the right; the pupils

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[1] *Loc. cit.*, p. 192.

[2] *Loc. cit.*, p. 500.

[3] *Rev. de Méd.*, Paris, 1883, III., 536.

[4] "Diseases of the Nervous System," London, 1876.

[5] *Jour. d. sci. méd. de Lille*, 1883, V., 321.

[6] *Progrès méd.*, 1884, August.

scarcely deviated from the middle line, and there was no nystagmus when the patient was asked to look towards that side; while movements to the left were performed easily, and at the same time very pronounced oscillations of the eyeballs occurred. Many cases, however, in which there is marked nystagmus fail altogether to show any weakness of the external ocular muscles, and nystagmus has been observed in a marked degree when the paralysis was slight and *vice versâ*. It seems more probable in many cases that we have to deal with a disturbance of co-ordination of the extrinsic muscles of the eye. The perfect bilateral symmetry of the nystagmus indicates its central origin, and the disturbance of co-ordination is probably brought about by the development of sclerotic patches in one or more of the various centres for the movements of the eyes. For lateral movements there is a separate centre in the pons on the side towards which the movement takes place, and this centre seems to be the one most usually implicated. Gowers[1] has known nystagmus to occur in disease localised to one side of the pons. In the *post-mortem* examination on three of my cases where nystagmus was present during life, the pons and medulla contained many sclerotic patches. Ferrier,[2] in a series of experiments, produced nystagmus by irritation of the cerebellum. In addition nystagmus is a frequent symptom of cerebellar tumour. The autopsies, however, on the three above-mentioned cases showed the cerebellum to be entirely free from disease.

*Strabismus.*—Uhthoff[3] has found paralysis of ocular muscles in 17 per cent of his cases. Double vision was complained of in seven out of my 33 cases of disseminated sclerosis, but in two of these no paralysis of any of the muscles could be detected. In the remaining five, the strabismus was well marked. Case I. first showed paralysis in the left internal rectus, and, later, in the right internal rectus also; in Case XIV. there was true paralysis of the right external rectus, and associated paralysis of the left internal rectus. On looking to the right the eyes could be brought up to, but not beyond, the

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[1] *Loc. cit.*, p. 193.

[2] "West Riding Lunatic Asylum Reports," 1873, Vol. III., p. 70.

[3] *Arch. für Psychiatrie*, Berlin, 1889, XXI., p. 55.

middle line. One naturally thought that a patch of sclerosis had involved the nucleus of the sixth nerve only; however, very extensive changes were found in the pons, and the nucleus of the third nerve was also implicated. This case also showed weakness in the right superior oblique muscle. Slight paresis of the right external rectus was observed in Case V., and in the remaining two cases there was strabismus of the left internal rectus. Diplopia is frequently complained of in early stages of the disease, and the weakness is usually partial and transient, passing off entirely after existing a short period. This may be due, as I suggested in discussing paresis generally, to shrinkage of the inflammatory exudation which has been pressing on the cells of the nucleus, or possibly in virtue of some movement of compensation. The later paralyses also, as a rule, are of central origin, but they may occasionally be due to sclerosis of a peripheral nerve.

*Iris.*—No great abnormality of the pupil was seen in my cases. In three instances the pupils were widely dilated; in Case XIV. they were unequal, another showed myosis, and in several the reflexes of the iris appeared to be brisker than usual. According to Perinaud,[1] inequality of the pupils during rest, equalised sometimes on movement, occurs in the early stage of the disease. Later myosis predominates, and this Perinaud regards as due to contracture, but he has noticed, however, that further contraction, on accommodation or exposure to light, takes place. The Argyll-Robertson phenomenon is excessively rare.

*Optic Nerve.*—Amblyopia is of frequent occurrence in disseminated sclerosis. Uhthoff[2] has remarked that, with the exception of cerebral tumours and tuberculous meningitis, there is no disease of the nervous system (even including tabes) which is so often accompanied by ophthalmoscopic changes, as disseminated sclerosis. He found the fundus oculi normal only in 48 out of 100 cases. Charcot[3] noticed ophthalmoscopic changes in 55 per cent of his cases; Buzzard[4] found pallor of the optic

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[1] *Loc. cit.*

[2] *Wien. klin. Woch.*, 1889, II., p. 787.

[3] *Progrés méd.*, Paris, March 14, 1892.

[4] *Brit. Med. Jour.*, Oct. 7, 1893.

discs in 43 per cent, and out of Gnauck's[1] 50 examples of the disease only 22 had no visual trouble. My own observations agree fairly well with the above, as 11 out of 33 cases complained of dimness of vision in one or both eyes. In four of these the discs seemed quite normal, but the other seven showed well-marked ophthalmoscopic appearances of atrophy, the discs being of a chalky-white colour, with small retinal vessels. In these seven cases, showing atrophy, both nerves were affected in four; in two, the left nerve was atrophic, and there was right optic atrophy in the remaining case. The atrophy met with in disseminated sclerosis is nearly always secondary to the development of sclerotic patches in the optic nerves, chiasma, or tracts. This was apparently so in five out of my seven cases, with ophthalmoscopic changes, as no optic neuritis could be made out while under observation. The atrophic whiteness in most of my cases seemed to be fairly uniform in distribution, but Gnauck[2] has asserted that the atrophy is quite commonly confined to the temporal two-thirds or half, and even if the nasal half becomes also affected, the temporal portions show the changes more markedly. More rarely the atrophy appears to be consecutive to neuritis. One of my cases, showing marked left optic atrophy, had unmistakable signs of early optic neuritis in the right eye. In Case V., one noticed right optic atrophy, while the left disc was white with an irregular, blurred, inner margin, and this latter was very probably the remains of an old neuritis. Uhthoff[3] states that in 25 per cent of his cases of disseminated sclerosis, with ophthalmoscopic changes, the atrophy was of neuritic origin, and he adds that the optic neuritis turns very rapidly into atrophy. This last observation may be the reason why optic neuritis is not oftener seen; it is not always possible to recognise the neuritic origin. Buzzard,[4] however, says that he has never in disseminated sclerosis seen true optic neuritis, although on several occasions he has noted dark-grey discoloration, somewhat resembling in tint hyperæmic cerebral grey matter. His explanation is that in most cases the inter-

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[1] *Berlin. klin. Woch.*, 1884, p. 421.

[2] *Ibid.*

[3] *Wien. klin. Woch.*, 1889, II.

[4] *Brit. Med. Jour.*, Oct. 7, 1893.

stitial neuritis occurs in the form of a patch situated some distance behind the globe, and it is only in the very rare cases where the lesion affects the nerve as it enters the globe that the discoloration is met with. Primary atrophy of the optic nerve in disseminated sclerosis is excessively rare, Gowers[1] having only met with four or five examples.

The visual impairment accompanying these atrophic changes varies very much. It is very often unilateral, and when bilateral is not symmetrical in the two eyes. Occasionally optic atrophy has been observed without visual disturbance, and this is probably accounted for by the escape of the axis-cylinders; on the other hand, visual troubles without ophthalmoscopic signs of atrophy, as in my four previously-mentioned cases, are commonly met with. In my cases the failure of vision came on gradually in all except one, but Uhthoff[2] noted a sudden onset in half his cases. The first symptom complained of in Case IV. and in Case VII. was dimness of sight, but as a rule visual troubles are not manifested till later in the disease. The visual disturbances are remarkable for their rapid changes; they may appear within a short period, attain their maximum rapidly, and may occasionally retrograde as quickly. They develop under two forms, the central and the peripheral scotoma, or rather limitation of the visual or colour fields. Perinaud[3] and Uhthoff[4] describe in detail the various alterations of the field of vision. The dyschromatopsy met with in disseminated sclerosis shows itself first by a disturbance in red and green followed by the disappearance of blue and yellow. A uni-ocular central scotoma for white, red, and blue has been observed by Habershon.[5] Very rarely indeed does the amblyopia go on to complete blindness. Magnan,[6] however, has described a case in which there was papillary atrophy of both eyes, with complete blindness. Gnauck[7] also has observed complete abolition of

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[1] *Loc. cit.*, p. 513.

[2] *Wien. klin. Woch.*, 1889, II.

[3] *Loc. cit.*

[4] *Archiv für Psychiatric*, Berlin, 1889, XXI.

[5] *Transactions of Ophthal. Soc.*, Vol. IX., 1889, p. 162.

[6] *Archives de Physiologie*, Vol. II., p. 765.

[7] *Loc. cit.*

vision in one case. In Liouville's[1] case patches of sclerosis occupied the whole thickness of the optic nerves, yet simply an enfeeblement of sight was noted. Again in Case IV. a section across either optic nerve showed a very slight amount of normal tissue only at the periphery (Fig. 16), yet vision was never by any means completely lost. This apparent disproportion between the symptom and the lesion constitutes, according to Charcot,[2] one of the most powerful arguments that can be invoked to show that the functional continuity of the nerve-tubes is not absolutely interrupted, although these, in their course through the sclerosed patches, have been despoiled of their medullary sheaths and reduced to axis-cylinders.

*Choroid.*—In Case VII., the presence of disseminated choroiditis will be noted. I cannot but think that it occurred quite independently of the disseminated sclerosis, yet no cause could be found for it. Most careful estimation of the refraction resulted in the finding of only a low degree of myopia, and repeated inquiries revealed absolutely no history of syphilis.

*Eyelids.*—Ptosis is rare, but has been noticed in cases by Charcot,[3] Sparks,[4] Zenker,[5] Gnauck,[6] and others. Ptosis was also observed in Case XIV. In Case V., there was noticed a peculiar tendency to close the left eye. It was not a ptosis, but was a screwing up, as it were, of the lids—a sort of spasm of the orbicularis palpebrarum. This same symptom was present in another of my cases of disseminated sclerosis, but there seems to be no mention made of it in the literature of the subject.

The following case is especially interesting as regards the eye symptoms.

Case V.—Isabella M., aged 21 years, was admitted as an in-patient at the Manchester Royal Infirmary under the care of Dr. Dreschfeld, March 7, 1894.

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[1] *Loc. cit.*

[2] "Diseases of the Nervous System." New Sydenham Society, 1887, Lect. VII., p. 191.

[3] *Progrès. méd*, Paris, March 14, 1891.

[4] *Loc. cit.*

[5] *Loc. cit.*

[6] *Loc. cit.*

*Previous Health.*—Three years ago she had influenza, which confined her to the house for over six weeks, and left her very weak. Her previous health has otherwise been good.

*Family History* unimportant.

*History of Present Illness.*—Twelve months ago patient suffered from severe occipital headache for one week. When this abated she noticed that she was unsteady in walking, and that her legs felt weak. She was able to continue at her work, however, until June, 1893, when she began to have trembling in her hands, arms, head, and legs. Her work consisted in stamping numbers on business and other books, and she was frequently reprimanded for stamping them in a crooked manner. But the greater her effort the worse was the result, and she was compelled to give up her work. Last July (1893) her sight began to fail, and about this time her speech became affected, and she experienced severe pains in her back, head, and arms. The trembling of the head became worse a month before admission, and her walking has gradually got more and more difficult, so that she has had to spend most of her time in the recumbent posture.

*Present Condition* (March 7).—The patient is well nourished and looks healthy. There is tremor of the whole body on voluntary movement, but the tremor is most marked in the head, neck, and hands. When the patient lies still in bed there is not the slightest tremor. The tremor in the head is most marked when she sits up, that in the neck when the head is thrown back. Attempts to drink out of a glass result in spilling of the water, and she has considerable difficulty in touching the end of her nose. She cannot walk without support. Both knee-jerks are exaggerated. Ankle-clonus is well marked on the right, but it is only slight on the left. There is no rigidity to passive movement. Nystagmus is obtained on lateral movements, the right external rectus exhibits slight paresis and she has sometimes double vision. She shows a curious tendency to close the left eye. There is well-marked atrophy of the right optic nerve, the disc being chalky-white and the vessels small; the left disc is also white, but presents an irregular blurred inner margin. The vision in both eyes is very bad, there being failure to read even large print. There is no hemianopia, and the pupils react to light and accommodation. Hearing, taste, and smell normal. The left naso-labial fold is better marked than the right, and when the teeth are shown the left angle of the mouth is retracted more than the right. The tongue can be well protruded. There is slight "scanning speech." The memory is very bad. No anæsthesia is to be found, but she complains of numbness in the right arm. The bowels are inclined to constipation. Bladder functions normal.

March 20.—Patient feels very well except for occasional attacks of giddiness.

April 2.—The tremors are more marked and the vision is worse.

April 30.—She is unable to raise the right leg from the bed.

May 10.—Some slight difficulty in micturition.

May 13.—Discharged—unrelieved.

The patient died at home on June 25, 1894, and unfortunately no autopsy was obtained.

**Bulbar Symptoms**—*Speech.*—Changes in articulation are very frequent. Only six out my 33 cases of disseminated sclerosis had not the characteristic speech of the disease; five of these spoke normally and the sixth presented only a slight drawl. Pritchard[1] found some abnormality of speech in 90 per cent of children suffering from disseminated sclerosis. Occasionally alteration of speech is a premonitory symptom of the disease. In cases by Bernhardt[2] and by Zimmermann,[3] hasty and precipitate speech was observed at the beginning of the disease.

In the speech of disseminated sclerosis the most striking characteristic is the well-known slow and laborious utterance in which, with evident effort, each sentence is enunciated separately and deliberately. This is the "staccato speech" of disseminated sclerosis. Sometimes it is termed "scanning speech," because the effect on the ear of the listener is not unlike that produced when some one is heard scanning deliberately a line of Latin poetry. The speech reminds one forcibly of the efforts of a child reading out of its primer, or repeating by rote what it does not understand. It is not, however, so distinct as a healthy person's accentuated speech. The words are often imperfectly pronounced, there is drawling of the syllables and frequent slurring over any letters or syllables which are difficult of pronunciation, or, as in a case by Radlick,[4] certain letters are replaced by others. When the "staccato" character is extremely

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[1] *Loc. cit.*, p. 500.

[2] "Real-Encyclopœdie der gesammten Heilwissenschaft," von Eulenberg, II. Anfl., Bd. VIII., p. 99.

[3] *Arch. of Ophthal.*, XX., 1891, p. 329.

[4] "Fall von sclerose en plaques," *Diss.*, Berlin, 1874.

well marked, some individual syllables may now and again be shot out with explosive violence. This was well seen in a case published by Schüle.[1] In one of my cases it was noticed that there were only a few words delivered on each breath, and this was apparently due to a rapid loss of breath by expiration during the intersyllabic pauses. In a case mentioned by Erb, [2] there was rhythmical alteration of notes at definite musical periods. As the disease advances the staccato element is apt to become less striking and the drawling and slurring more and more marked, until at last speech is reduced to an inarticulate drawl. In the later stages the voice often becomes weak and whispering.

Leube[3] examined the larynx of a case of disseminated sclerosis, with "scanning speech," and found that the vocal cords could be brought together, but that their tension soon relaxed and frequently changed. Krause[4] has also found relaxation of the vocal cords in a remarkable manner to underlie the change in phonation. Permewan,[5] however, has examined cases of disseminated sclerosis, with voice alteration, and found the laryngeal muscles unaffected. Krzywicki[6] mentions a case which is especially noteworthy, from the fact that the muscular elements of the larynx were analogous to those of the extremities. Tremors of the glottis occurred, and the adductors and tensors were markedly weaker than the abductors. In several of my cases there was marked fibrillary trembling of the tongue; in another case the tongue was protrnded in a very jerky fashion with considerable difficulty, and at two attempts, and, lastly, another case showed slight tremor and loss of mobility of the lips. Tremors of the tongue were seen in cases of the disease in children reported by Wilson,[7] Hoedemaker,[8] and Cheadle ;[9] in

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[1] *Loc. cit.*

[2] *Loc. cit.*, p. 497.

[3] *Deutsches Archiv f. klin. Med.*, Bd. VIII., S. 1, 1870.

[4] *Neurologisches Centralblatt*, 1885.

[5] *Journal of Laryngology*, Oct. 1894, p. 652.

[6] *Deutsches med. Woch.*, Leipzig, 1892, March 24.

[7] *Brit. Med. Jour.* 1876, II., p. 675.

[8] *Deutsches Archiv f. klin. Med.*, 1879, XXIII., p. 443.

[9] *Med. Times and Gaz.*, Feb. 9, 1873, p. 139.

both tongue and lips in a case by Bristowe.[1] The slow staccato utterance of disseminated sclerosis is believed to be due to the interference with conduction in the motor speech tracts, that is produced by the compression of the nerve fibres at points where they are passing through patches of sclerosis. In the purely spinal form of the disease, articulation—to judge from a few cases—does not appear to suffer. The characteristic speech has been present when there has been perfect integrity of the bulbar nuclei and basal conducting fibres, but extensive sclerotic change in the corona radiata has been found seriously interfering with the tracts along which impulses are conveyed downwards from the cortex cerebri. This was so in a case published by Jolly.[2] Leube[3] has thought that the speech was due to weakness of the vocal cords, so that their capacity was only equal to the production of isolated syllables, and Duchenne has ascribed the speech to a twitching of the diaphragm. These views, however, seem most improbable.

Though "staccato" utterance is most typically exhibited in disseminated sclerosis, it would be a mistake to suppose that it occurs only in that disease. An element of "staccato" utterance in often present in the speech of general paralysis of the insane, and it is met with also in the speech of some aphasic patients when they are beginning to regain the powers of speech by training the convolutions of the opposite hemisphere. Scanning speech is also seen in Case IX., which is most probably an example of Friedreich's disease; it is said also to occur sometimes in locomotor ataxia, and it was present in Gray's[4] case of lepto-meningitis cerebri.

*Other bulbar symptoms* are occasionally seen. Ebstein[5] relates a case in which there was marked atrophy of the anterior portion of the tongue, and after death a sclerotic patch was found involving the nucleus and fibres of origin of the hypoglossal nerve. True bulbar paralysis is rare, but was

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[1] *Ibid.*, June 21, 1878, p. 673

[2] *Loc. cit.*

[3] *Loc. cit.*

[4] *Loc. cit.*

[5] *Loc. cit.*

well seen in Dr. Dreschfeld's[1] two examples of the disease in children, and it was the cause of death in Schüle's[2] case. Other cases, showing labio-glosso-pharyngeal paralysis are related by Leube,[3] Joffroy,[4] Bourneville,[5] and others. In Case I. there was occasional regurgitation of fluids through the nose. As a rule death soon takes place after the supervention of bulbar paralysis, and difficulty of swallowing, paroxysmal dyspnœa (Charcot), broncho-pneumonia, and cardiac failure may then be the immediate cause of death. In Dr. Dreschfeld's two cases, however, the paralysis existed from the onset, and yet showed but little advance years afterwards.

**Affections of other Cranial Nerves.**—Several of my cases presented deafness coming on gradually. In one the deafness was an initial symptom, and was on the left side; in another it occurred late in the disease, and was also on the left. A third case—a girl under the care of the late Dr. Ross—had deafness on the right side, together with marked impairment of taste. In none of these cases were there any signs of middle or external ear disease. Deafness in the left ear was an early symptom in Bastian's[6] case, later deafness appeared on the right ear, and finally became absolute on the right side. Deafness was also seen in cases by Drummond,[7] Edge,[8] and Moxon[9]—in the case of the latter it was only temporary. One of my cases presented well-marked facial paralysis on the left side, and right facial paralysis was observed in Case V. Facial paralysis also occurred in Schüle's[10] case. The sense of smell did not appear to be affected in any of my cases. I examined the olfactory lobes in two cases after death, but found them free from disease. The deafness and facial paralysis probably depend upon sclerotic patches, involving the nerve-nucleus, or the nerve itself, in some part of its course.

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[1] *Loc. cit.*
[2] *Loc. cit.*
[3] *Loc. cit.*
[4] *Gaz. méd. de Paris*, 1870, Nr. 23.
[5] Charcot's "Diseases of the Nervous System," Lect. VIII., p. 215.
[6] *Loc. cit.*
[7] *Lancet*, 1887, I., p. 13.
[8] *Ibid*, 1885, II., p. 568.
[9] *Loc. cit.*
[10] *Loc. cit.*

**Psychical Disturbances** are common features of the disease. According to Ross[1] they are always observed in disseminated sclerosis. Psychical troubles were seen in 12 out of 14 published cases in children collected by Marie,[2] and in 8 out of my 33 cases of the disease the patients were very emotional. They would frequently break out into paroxysms of laughter, which showed no relation to humour. On the other hand they would be seized with incontrollable fits of weeping, apparently without the slightest cause. This symptom came on early in the above cases, but got more marked as the disease advanced. Oppenheim[3] looks upon this involuntary laughter or weeping as an independent symptom, and not a psychical anomaly. He has met with it in multiple cerebral hæmorrhage, and in patches of softening. Persons suffering from disseminated sclerosis often manifest undue contentment with their unfortunate condition. Cases I., V., and several others were particularly happy; on the other hand Cases VI. and XIV. were very miserable. An intermediate stage between these two extremes was seen in Case IV., where the patient was neither very depressed nor very cheerful. The undue contentment differs very much from the mental condition seen in phthisis—in disseminated sclerosis it amounts to indifference as to the future progress of the disease; there is not the buoyant hopefulness which is noticed in phthisis. Gowers[4] thinks that the morbid complacency is more frequent in women than in men, but in my cases it seemed to be fairly equally distributed. Catsaras[5] publishes a case of disseminated sclerosis in which a very peculiar psychical state was observed. It consisted of an irresistible tendency on the part of the patient to seek everywhere for something, without being able to tell precisely what he was looking for, although he had full knowledge of what he was doing. Thus, he opened a cupboard, examined its contents carefully, and, not chancing to find what he was looking for, he went to another part to continue his search.

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[1] *Loc. cit.*, p. 759.

[2] *Revue de Méd.*, Paris, 1883, III., p. 536.

[3] *Charité-Annalen*, 1889, p. 413.

[4] *Loc. cit.*, p. 514.

[5] *Archiv. de Neurol.*, 1885, X., p. 72.

As regards facial expression, at least six of my cases presented a vague and uncertain expression, or rather, want of expression; the features seemed hanging and deficient in mobility. On conversation, however, these patients were very intelligent, much more so than they looked. Others had a sleepy, languid, somewhat stupid appearance. Many of them, in other respects, looked the picture of health, at any rate, up to the final stages of the disease. The term, "*air de béatitude*," has been given to the facial expression of disseminated sclerosis. In children a large drooping lower lip has been frequently noticed.

The intelligence is almost invariably defective sooner or later in the disease at all ages. The defect is more noticeable in children, because the child's psychical centres have never been stored with impressions. In my adult cases, the impaired intelligence seemed to be due partly, at any rate, to loss of memory. None of my cases showed any greater degree of mental disorder, but several isolated examples of the disease are related in the literature of the subject, where the failure of the mental faculties has gone on to complete insanity. Melancholia, accompanied by stupor and refusal of food, has been noticed by Erb,[1] Charcot, Bourneville and Guérard,[3] and others. Charcot[4] reports the case of a female patient, in which was present the singular combination of disseminated sclerosis and general paralysis of the insane. Other cases of disseminated sclerosis, presenting symptoms of general paralysis, are recorded by Leube,[5] Valentiner,[6] and others. In Schüle's case, the child fell into a complete state of imbecility. Cases of monomania, and various forms of mania, have been described, and some of these have gone on to chronic dementia. The psychical symptoms are undoubtedly referable to patches of sclerosis in the cerebral hemispheres, but as yet, however, anything like the exact relations of the specific localisations of the patches to the particular form of psychical dis-

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[1] *Loc. cit.*, p. 500.

[2] *Loc. cit.*, p. 195.

[3] *Loc. cit.*, p.92.

[4] *La Semaine Médicale*, Paris, 1892, January 27

[5] *Loc. cit.*, p. 14.

[6] "Ueber Sklerose des Gehirns und Rückenmarks." *Deutsche Klinik*, 1856, No. 14.

turbance has not yet been discovered. In several of my cases, which clinically displayed little or no mental disorder, there was found, on *post mortem* examination, a considerable number of sclerotic areas scattered throughout the hemispheres. Case IV. was always very intelligent, and at the autopsy no nodules could be discovered in the cerebrum proper. Bevan Lewis[1] describes a case of disseminated sclerosis, in which acute delirious mania appeared; the autopsy showed very numerous sclerotic areas, especially in the white matter of the frontal lobes.

**Headache and Vertigo.**—Attacks of headache and giddiness often occur in disseminated sclerosis. Of my 33 examples of the disease 16 showed well-marked vertigo, and 10 frequently complained of severe headache. Vertigo is very frequently mentioned in published cases. Charcot[2] says that it is found in three-quarters of all cases of the disease, and that it nearly always is of the gyratory variety, the patients feeling as if they were turning round, or else surrounding objects appearing to do so. Should diplopia be present, it may cause a visual vertigo. The vertiginous attacks are usually met with early in the disease, and disappear in the later stages. When severe, they may be accompanied by vomiting.

**Apoplectiform attacks** are said to be not at all rare in disseminated sclerosis, occurring, according to Charcot,[3] in about a fifth of the total cases. None of my cases, however, suffered from these peculiar seizures.

After, as a rule, slight premonitory signs, there is a sudden development of severe cerebral symptoms. The patient usually becomes more or less completely unconscious, or even deeply comatose. This loss of consciousness is accompanied by some form of paralysis, considerable elevation of temperature, very rapid pulse, and a markedly flushed face. The paralysis is usually of a hemiplegic character, but may show various other forms. Dr. Edge[4] publishes the case of a man, afflicted with

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[1] *Journal of Mental Science*, XXIII., January, 1878, p. 564.

[2] "Diseases of the Nervous System." *New Sydenham Society*, 1877, Lect. VII. p. 194.

[3] *Ibid.*, p. 204.

[4] *Loc. cit.*

disseminated sclerosis, who had repeated apoplectiform seizures. In one attack there was slight hemiplegia, without implication of the face; at another time, paraplegia; on the next occasion all the extremities were involved, and in the last attack left hemiplegia, with implication of the face. The temperature usually rushes quickly up to 103° F., or, in exceptional and fatal cases, it may reach 108° F, or 109° F. In Charcot's[1] experience, a temperature above 104° F. is almost always followed by a fatal termination; in Dr. Edge's case, however, recovery ensued after so high a reading as 105·6°. Consciousness is not always lost in these attacks; Dr. Edge's patient was unconscious in all the seizures except the last. The typical attacks generally last 24 to 48 hours, or longer; then consciousness reappears, the temperature falls, and a deep sleep supervenes from which the patient awakens comparatively well. The intervals between the attacks vary considerably. The seizures are not as a rule fatal, but may be so, as in cases published by De Fleury,[2] Moxon,[3] and others; but, nevertheless, each attack marks a distinct forward step in the morbid process. Very occasionally, disseminated sclerosis is ushered in by an apoplectiform seizure (see "Onset"). Apoplectiform attacks are not often mentioned in examples of the disease in children. Hoedemaker,[4] however, relates the case of a girl of 10 in which a typical attack occurred, there being left hemiplegia, raised temperature, and a complete state of torpor.

These seizures are by no means peculiar to disseminated sclerosis. Precisely similar attacks frequently occur in general paralysis of the insane, and they have occasionally also been seen in tumours of the brain, and in cases in which embolic softenings or apoplectiform effusions have left chronic lesions behind them. The cause of the attacks is very obscure. Autopsies in cases of death during an attack have revealed nothing but old changes. Charcot[5] could never discover either œdema or acute hyperæmia of the brain. It has been suggested

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[1] "Diseases of the Nervous System." *New Sydenham Society*, 1877, p. 207.

[2] *Revue de Méd.*, Paris, 1885, p. 314.

[3] *Loc. cit.*

[4] *Loc. cit.*

[5] "Diseases of the Nervous System." *New Sydenham Society*, 1877, p. 205.

that they perhaps indicate the acute development of new sclerotic patches; but one would expect them in that case to be much more common. Charcot[1] says that they are only met with in cases where the pons and medulla are involved, either primarily or secondarily. Several of my cases showed marked sclerosis of these regions, yet no apoplectiform or epileptiform seizures appeared from first to last.

**Epileptiform attacks** are mentioned by Charcot[2] and others as occurring in disseminated sclerosis. They are analogous to the epileptiform attacks which are met with in general paralysis of the insane, and have been observed in adult cases by Kelp,[3] Husch,[4] and Leube.[5] The frequency with which convulsive seizures inaugurate the disease in early life is rather remarkable. They have been observed in more than half the cases recorded. The well-known susceptibility to eclampsia in infancy and childhood affords a partial general explanation of their presence in this disease; but the relationship is decidedly more than a mere coincidence in the majority of cases. It is still discussed by some whether the convulsions are merely premonitory symptoms or are actual causal factors of the disease. In six out of Marie's[6] fourteen collected cases repeated convulsive attacks occurred during the course of the disease.

**Trophic Disorders.**—*Muscular atrophy* is very rarely seen except in the later stages of the disease. In all my cases, excepting Case I., it was entirely absent. In the latter case, reaction of degeneration was obtained in the left gastrocnemius, the tibialis antici, the peronei, and the long flexors of the toes; but no muscular atrophy could be detected in the arms, neck, face, or tongue. It seems to me remarkable that the ganglion cells in the anterior horns of the cord should resist for so long a time the often extensive sclerotic process. For instance, in Case IV., the sclerosis almost completely

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[1] *Ibid.*, p. 205.

[2] *Ibid.*, p. 206.

[3] *Loc. cit.*

[4] *Deutsches Arch. f. klin. Med.*, 1870.

[5] *Loc. cit.*

[6] *Revue de Méd.*, Paris, 1883, III., p. 536.

involved the whole transverse section of the cord, and yet there was no true muscular atrophy. There was, however, in this case, as well as others, general wasting of muscle following disuse, but no reaction of degeneration was obtained. Among published cases, also, muscular atrophy is very seldom noticed. It was, however, present in cases by Westphal,[1] Hoedemaker,[2] and Dickenson.[3]

*Skin Lesions.*—Bedsores are very frequently met with in disseminated sclerosis as in chronic cord disease generally, when the final stages are at all prolonged. In Case I. and Case V. the bedsores were very extensive, but no other skin lesion was seen in my cases. I was unable to discover, in three cases, any signs of sclerosis in the posterior nerve roots. As the nutrition of the skin seems to depend on nerves that have their course in the posterior roots, one would not expect skin lesions in disseminated sclerosis, or, if at all, only in late periods of the disease, sclerosis of the posterior roots being secondary to that of the cord. Herpes zoster was noticed in a case by Sparks,[4] changes in the growth of the nails by De Fleury,[5] and altered secretion of sweat and alopecia have also been observed.

*Changes in the Bones and Joints.*—Bourneville[6] mentions cases where softening of bone, cyphosis, scoliosis, and effusion of fluid into joints had occurred.

**Vasomotor Disturbances** occasionally occur, and appear to be due to sclerotic patches involving the vaso-motor centres in medulla and cord. In a case published by Bastian,[7] the so-called "tache cérébrale" and factitious urticaria could be easily produced almost throughout the disease; the medulla was very extensively implicated. In Dr. Edge's[8] case, also, there was a

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[1] *Charité-Annalen*, 1887, Bd. CXIII., p. 454.

[2] *Loc. cit.*

[3] *Medical Times and Gazette*, December 29, 1877, p. 692.

[4] *Loc. cit.*

[5] *Loc. cit.*

[6] "Charcot's Lectures on Diseases of the Nervous System."—*New Sydenham Soc.*, 1877, p. 213.

[7] *Loc. cit.*

[8] *Loc. cit.*

temporary vaso-motor disturbance; the extremities became perfectly cold to the touch, and the forearms assumed a reddish-purple colour. Bourneville and Guérard[1] quote a case of disseminated sclerosis where the forearms and hands were permanently of a purple tint and somewhat œdematous, the temperature of the parts being normal.

**Affections of the Genito-Urinary Organs.**—Disseminated sclerosis, by its localisation in the floor of the fourth ventricle, frequently gives rise to special urinary troubles. These consist of simple polyuria, diabetes insipidus, glycosuria, and true diabetes. According to Claude Bernard and others, puncture of the middle of the space included within the origin of the pneumogastric and auditory nerves causes both an increase in the quantity of the urine, and the appearance of sugar in that fluid. If one punctures a little higher, the urine is less abundant, less charged with sugar, but often contains albumen. The polyuria, glycosuria, and albuminuria can all be produced separately and independently of one another. Claude Bernard, however, never succeeded in producing, by puncture of the medulla, more than a temporary glycosuria lasting for 48 hours at most—never a permanent disease. When, however, glycosuria is produced by a sclerotic patch it is usually permanent or occasionally intermittent.

In the case of a woman of 26, published by Husch,[2] diabetes insipidus continued throughout the disease. The autopsy confirmed the diagnosis of disseminated sclerosis.

Glycosuria was observed in one of my collected cases. A man of 25, an in-patient at the Manchester Royal Infirmary in 1880, under the care of Dr. Dreschfeld, presented well-marked intention tremor, especially in the upper extremities, marked nystagmus, slight drawl of the speech, inco-ordination and weakness of the lower extremities, commencing optic atrophy, and deafness on the left side coming on gradually without middle or external ear disease. He was very emotional and suffered considerably from vertigo and headache; the appetite was good, but not excessive, and there was no particular thirst. The urine had a specific gravity of 1030, and its quantity was considerably increased. The amount of sugar was very

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[1] *Loc. cit.* [2] *Loc. cit.*

variable, sometimes it was exceedingly slight, at other times abundant. An anti-diabetic diet produced no effect on the quantity of sugar.

Richardière[1] quotes a typical case of disseminated sclerosis in a man of 43, in which intermittent glycosuria was observed. The quantity of urine varied from 5·5 to 8·25 grammes of sugar in the litre, and the daily quantity of urine was a litre and a half.

Drummond[2] relates the case of a boy of eight, in which the urine was of large quantity, and contained sugar, but there was no other symptom of diabetes. At the autopsy, disseminated sclerosis was found, and one of the patches involved the centre of the floor of the fourth ventricle, implicating Claude Bernard's diabetic point.

Weichselbaum[3] publishes the case of a man of 34, who, on admission into hospital, was found to be wasted and anæmic. The skin was dry. The daily quantity of urine passed varied between 2,500—9,600 c.c.; the specific gravity was 1030, and the quantity of sugar was 5·4 per cent. At the autopsy, sclerotic patches were found in the three regions of the cord, the medulla, left optic thalamus, left external capsule, and both frontal lobes. Both kidneys and the muscular coat of the bladder were hypertrophied. In the floor of the fourth ventricle were found two sclerotic patches: one a round gelatinous dark-grey patch on the right side, half a centimetre in diameter and three millemetres deep, extended backwards to the ala cinerea, and forwards to the striæ acousticæ—the striæ acousticæ passed over the patch; a second patch of similar size, of more gelatinous appearance and of clearer colour in front of the striæ acousticæ on the right side, extended from the longitudinal sulcus outwards to the right locus cæruleus.

Edwards[4] quotes the case of a man of 31, diagnosed by Charcot as a case of disseminated sclerotis, who, while at the Salpêtrière, was found to be passing 180 grammes of sugar in 10 pints of non-albuminous urine per diem. There was much thirst and considerable appetite, yet loss of flesh. The quantity of sugar was not influenced by diet.

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[1] *Revue de Méd.*, IV., 1886, p. 622.

[2] *Loc. cit.*

[3] *Wien. med. Woch.*, 1881, No. 32.

[4] *Revue de Méd.*, Paris, 1886, VI., p. 703.

Considering how often the floor of the fourth ventricle is affected in disseminated sclerosis, it seems to me remarkable that we should so seldom get polyuria, albuminuria, or glycosuria. An interesting fact to be gleaned from these cases is that the knee-jerk remained increased, therefore much more than counterbalancing the tendency to the absence of knee-jerk, which is so often found in diabetes.

The *bladder* was frequently affected in my cases. Thus, in 4, there was marked retention of urine; in 6, the retention was slight, amounting to little more than hesitation; in 1, there was marked incontinence; in 7, there was slight incontinence at times; and in 15, the functions of the bladder were normal. In many of these difficulty of micturition came on early, but remained slight for a considerable time. Charcot[1] and others look upon affections of the sphincters as rare. I must conclude from my cases that disturbances of the bladder functions belong to the usual symptoms of disseminated sclerosis during the whole clinical history. They are mostly not permanent, but intercurrent and remittent symptoms. Oppenheim[2] states that of 35 cases which have come under his observation, affection of the bladder was seen in 80 per cent. Four of my cases developed cystitis, and this was partly the result of trophic disturbance. Pyelo-nephritis was also seen at the autopsies on four cases, and was due to the spreading upwards of the septic process in the bladder.

*Rectum.*—The rectal functions are also frequently affected. Slight constipation was noticed in the earlier stages of 12 of my collected cases. This, I think, to a considerable extent is due to the sedentary life that has to be led by sufferers from disseminated sclerosis. In 4 there was very marked constipation, or retention of fæces. In 3 there was incontinence of fæces, and in another the same was noted, but only in a slight degree. In the remaining 13 the bowels acted fairly normally. It is interesting to note how closely agreed are these analyses of the bladder and rectal functions.

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[1] "Diseases of the Nervous System."—*New Sydenham Soc.*, 1877, Lect. VII., p. 197.

[2] *Charité-Annalen*, 1889, p. 413.

The *sexual functions* were not investigated in my cases. According to most authorities they remain normal for a comparatively long period of time, but Ross[1] says that in some patients sexual desire appears to be increased at an early period of the disease, while in others it is completely abolished.

**Bodily Development.**—Occasionally, when the disease occurs very early in life, it appears to be accompanied by general retardation of growth. This was well seen in a case published by Pollard.[2] In Humphrey's[3] case, however, the child was very large for its age, the bones massive, and the muscles finely developed. The small stature appears to be akin to that of birth palsies.

The respiratory, circulatory, and digestive organs usually perform their respective functions normally up to the last stages of the disease. Inflammatory affections of the respiratory organs are then commonly met with. Attacks of syncope and severe palpitation have been noticed in several cases by Bourneville,[4] and gastric crises by Zenker.[5]

Some writers discriminate between cases in which the lesions are limited to or are most intense in the spinal cord, and those in which the brain is chiefly or exclusively involved, and hence they speak of a spinal, a cerebral, and a cerebro-spinal form. Complete limitation of the disease to the brain only seems to be very rare, and in these cases tremor is said to precede paralysis, and mental disturbances are prominent. Examples of purely cerebral disseminated sclerosis are related by Bourneville,[6] Kelp,[7] Bevan Lewis,[8] and Jolly.[9] Cases where the disease is limited to the cord only are not uncommon.

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[1] *Loc. cit.*, p. 758.

[2] *Loc. cit.*

[3] *Loc. cit.*

[4] "Nouvelle étude sur quelques points de la Sclérose en plaques disséminées," Paris, 1869.

[5] *Loc. cit.*

[6] "Nouvelle étude sur quelques points de la sclérose en plaques disséminées,' Paris, 1869.

[7] *Loc. cit.*

[8] *Loc. cit.*

[9] *Loc. cit.*

## CHAPTER III.

### ANOMALOUS CASES OF DISSEMINATED SCLEROSIS.

IN a certain, happily small, proportion of cases the disseminated patches of sclerosis in the central nervous system apparently fail to produce any of the characteristic signs of the disease. These cases, by the unusual behaviour of their symptoms, are frequently so difficult of diagnosis that it is often impossible, with any degree of certainty, to go further than make a probable conjecture as to their nature. One cannot but come to the conclusion that processes, apparently similar in nature and extent, do not always produce the same symptoms. It is more especially where the sclerotic patches are chiefly situated in the cord that the clinical translation of these patches appears under the mask of another nervous disease.

Charcot[1] classifies the atypical forms into (1) those which are abortive owing to the disappearance of the symptoms. They are usually of the spastic paraplegic type. (2) Those abortive, owing to early arrest of development of the disease. These, also, are of the spastic paraplegic type. (3) Those abortive on account of the supervention of unusual symptoms. These are subdivided into (*a*) the hemiplegic type, (*b*) the tabetic type, (*c*) the lateral amyotrophic type.

Clinical signs of disseminated sclerosis may be **very latent.** There are many cases, especially of the so-called "hysterical type," in which the patient, for long periods of time, only complains of slight subjective symptoms. This is well seen in the earlier history of Case VI.; but there are a few rare instances on record in which slight symptoms have alone appeared throughout the course of the disease. Strumpell[2] has seen one case in which, for a long time, the only symptom

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[1] *Progrès Méd.*, Paris, March 14, 1891.

[2] *Loc. cit.*

was a complaint of slight headache; there was then a slight transitory apoplectiform attack; several months later an epileptiform attack, and a few days after that death took place. Spitzka[1] had a case which for years he regarded as one of spinal irritation; then optic atrophy came on, and this was succeeded by unmistakable symptoms of disseminated sclerosis.

In other cases the disease may appear under the type of a **spastic paraplegia**. The following case, during its latter period, presented a condition of "spastic paraplegia":—

Case VI.—Agnes H., aged 35, single, was admitted as an in-patient at the Manchester Royal Infirmary, under the care of Dr. Bury, on May 24, 1894.

*Previous History.*—For the last seven years patient has been dress-making. Previously she was "behind the counter" from the age of 14, and had to endure much standing and long hours. She had scarlet fever when four years old, but otherwise has had no acute illness. No history of syphilis.

*Family History.*—She knows of no similar disease among any of her relatives. Her father is a martyr to gout, and her mother died in child-bed 31 years ago. No rheumatism in the family.

The *present illness* dates from 10 years back, when the patient's left hand became feeble. It remained so for a month, and then apparently completely recovered its power. Six years ago she suddenly felt a weakness in the left leg while walking, but this disappeared in a few minutes on resting. Since then she found that in walking any long distance the loss of power would return, and the intervals at which this took place gradually got shorter. She had no pain anywhere. In the middle of June, 1893, the right leg became affected somewhat suddenly, and has since gradually got weaker. Once or twice weekly since June she has had difficulty in holding her water, and generally the urine has dribbled away when she was walking about. There has been loss of control over the motions also. Since Christmas, 1893, the right hand has become weak.

*Present State* (May 24, 1894).—Patient is a healthy-looking woman. She cannot stand or walk alone. With assistance she walks with a spastic gait, and scrapes her toes on the ground. She cannot raise her left leg from the bed nor dorsiflex the left foot; she can slightly bend the right knee and hip, but not the right ankle. No atrophy of the

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[1] *Loc. cit., p.* 880.

muscles of the leg. Passive movement reveals the existence of slight rigidity in both legs, but this is more marked in the left. Both knee-jerks are increased and ankle-clonus is well marked on both sides. The plantar reflex is present on either side, but the abdominal and epigastric reflexes are not obtained. There is no numbness in the legs, and the patient can feel and localise the touch of a pin's head, and can differentiate between the head and point of the pin all over the body. No pain in the head, legs, or back. The grasp of both hands is fairly powerful, but the right seems a little weaker than the left ; the movements of the arms are good. There is a slightly prominent third dorsal spine, but it exists without pain or tenderness. No nystagmus. Vision good, and ophthalmoscopic examination negative. She presents no sign of paralysis in the facial, ocular, or tongue muscles. The patient, on being questioned, states that she has occasionally had slight trembling—not increased on movement—in her hands, but whilst in hospital not the slightest trace of tremor was seen. Speech normal. The bladder is distended, and there is dribbling of urine. No control over the motions.

May 30.—The bladder has been distended for several days, reaching almost to the umbilicus. Catheterism was begun.

June 3.—Urine cloudy, of specific gravity 1018, alkaline, and ammoniacal. Numerous pus cells and a few blood corpuscles present.

June 4.—The patient is gradually lapsing into a semi-comatose condition. She would answer questions for a time, but became by degrees more and more comatose.

June 5.—She is quite unconscious this morning. The pulse is 168, respirations 40, and the face flushed and perspiring. The pupils are equal, and react to light, and the corneal reflex is present. Head and eyes turned to the right to a small extent. There have been no true convulsions, but occasional twitchings of the limbs have occurred, and in the night she moved her head backwards at intervals of a minute or so.

June 6.—Still quite unconscious ; the face is flushed, and the conjunctivæ congested. There is conjugate deviation of the eyes to the right. Cheyne-Stokes' respiration. Pulse 176, and very feeble, temperature 101·5°. Knee-jerks present, and there is ankle-clonus on both sides. When the arms are raised, they both fall down the moment they are released. There is no evidence of weakness of one side, nor is there any facial paralysis. The patient died the same evening.

The *post-mortem* examination, which revealed the presence of typical disseminated sclerosis, will be related in Chapter V.

Charcot[1] relates a case of this type of which the following is a summary :—

The patient, a woman of 36, gave a history of general and gradual enfeeblement of the limbs commencing 14 years ago. Since then she has had vertigo, slight trembling of the hands not increased on movement, transitory blindness, double vision, remissions, repeated trepidation of the lower limbs and lightning pains.

On admission (July, 1877) she had paresis of the upper limbs without tremor. Lower limbs paralysed and a little rigid. Legs drawn into semiflexion by temporary contractures. Knee-jerks exaggerated with ankle-clonus on both sides. Involuntary passage of urine. In October, 1877, she developed an external strabismus of the right eye. In January, 1878, there was marked rigidity of the legs. In March, 1878, bedsores formed, followed by erysipelas and death. At the autopsy numerous sclerotic patches were found in the different parts of the brain and spinal cord—the whole transverse section of the dorsal region was sclerosed, the posterior columns in the lumbar and upper cervical regions, and the left lateral column in the lower cervical.

The history in this case was of great value, for when Charcot showed the woman in a clinical lecture, she presented simply a condition of spastic paraplegia.

Another very similar case is reported by Bonicli.[2] A man of 23 on admission into hospital presented the following symptoms: Rigidity and paralysis of the legs, exaggerated knee-jerks with ankle-clonus and the plantar reflex present on both sides. The upper extremities normal. No intention tremor, no nystagmus, no affection of sensibility, bladder and rectum normal, considerable hypertrophy of the subcutaneous fat. Later "scanning speech," amblyopia, and loss of memory were noticed. Finally there were bedsores and very troublesome constipation. The autopsy showed patches about the cerebral ventricles, in the corpus callosum, crura, pons, medulla, and cord. The patches were confluent in the lower part of the cord.

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[1] *Progrés Méd.*, Paris, Feb., 1879, No. vi., p. 97.

[2] *Archiv. de Neurol.*, 1885, I., p. 51.

Gnauck[1] also relates an example of the spastic paraplegic type.

Occasionally disseminated sclerosis has appeared under the clinical disguise of **amyotrophic lateral sclerosis.**

In the case of a woman of 46, published by Dejerine,[2] there was seen exceedingly pronounced paralysis and atrophy of the muscles of all four limbs and of the trunk. This came on first in the legs. There was also permanent contraction of the paralysed muscles, and, in addition, extremely severe attacks of contracture from time to time; these latter contractures were so severe as to throw the patient into a state of opisthotonus, and any attempt to make the limbs yield would have resulted in a fracture. There was integrity of the general and special sensibility and of the sphincters. Exaggeration of the tendon-reflexes and ankle-clonus present on both sides. Several months before death symptoms of bulbar paralysis came on: difficulty of articulation; a sardonic look produced by atrophic paralysis, with contracture of the lower half of the face, causing an exaggeration of both naso-labial folds; no atrophy of the tongue, and no respiratory or cardiac troubles. Gluteal bedsores then formed, followed by death after five years' illness. At the autopsy sclerotic patches were found in the brain, medulla and cord. There was integrity of the roots and trunks of the cranial nerves, also of the anterior and posterior spinal nerve-roots. Absolute integrity of the intra-muscular nerves. Simple atrophy of the muscles. Marked atrophy and pigmentation of the motor cells in the anterior cornua.

It would be exceedingly difficult to diagnose disseminated sclerosis in a parallel case.

Another case of disseminated sclerosis presenting the symptoms and the progress of amyotrophic lateral sclerosis is related by Killian.[3]

The patient was a man born in 1813. Weakness commenced in the legs, and was accompanied by pain, which was worse at night. The pain ceased, but the weakness increased

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[1] *Neurologisches Centralblatt*, 1884, p. 315.

[2] *Rev. de Méd.*, 1884, Bd. IV., p. 193.

[3] *Archiv für Psychiatric*, Bd. VII., 1877, p. 28.

rapidly, and he required a stick to get about, then two sticks, and then had to give up his work. The difficulty of walking increased, and the pain returned. Involuntary contractions of the right leg appeared, so that this leg was drawn up on the body when the patient was in bed. Soon after the left leg became similarly affected. When in the hospital at Strasbourg he was mentally stupid and indifferent to his surroundings. The legs were contracted in the flexed position, and there was also great rigidity and wasting of the legs. The wasting was particularly marked in the calf muscles, the thigh muscles being only moderately wasted. Fibrillary contractions were not observed. There was not complete analgesia, but the stupidity of the patient prevented minute examination. Elbows flexed. Marked atrophy of forearms and hands, muscles of ball of thumb and little finger much wasted, interosseous spaces abnormally deep. Muscular rigidity in arms, not so marked as in legs. No "scanning speech," tremor, or nystagmus. No real incontinence of urine and fæces. At the autopsy patches of sclerosis were found scattered in the roof of the lateral ventricles, and in the posterior part of the right optic thalamus. In the cord the sclerosis also corresponded in its situations to disseminated sclerosis, and there was no definite ascending or descending degeneration.

The case of Pitres[1] also presented symptoms in the upper limbs analogous to the two former cases. A woman of 53, on admission, showed complete paralysis of the upper limbs, with slight contracture. Muscular atrophy of the hands, less marked than the other parts of the upper limbs. Faradic contractility diminished. The lower limbs are paralysed, but the muscles are flaccid, and there is no ankle-clonus. The autopsy showed cerebro-spinal sclerosis in patches, and the muscles presented simple atrophy.

In very exceptional cases where the patches are localised to an unusual extent in the pons and medulla, the disease may simulate **chronic bulbar paralysis**.

Sometimes the disease appears under the mask of a **chronic myelitis**. There is a gradually increasing paraplegia of the legs, with vesical disturbance, loss of sensibility, etc.

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[1] *Revue Mensuelle*, Tome I., 1877, p. 893.

Morris[1] relates the case of a man in which the first symptoms were numbness and a feeling of heaviness in the left leg; this very gradually increased, and then the right leg was similarly affected. Walking now became impossible. Later weakness and partial loss of sensibility attacked first the left and then the right arm, so that all four limbs became paralysed, and showed anæsthesia, but the latter was never complete. Retention of urine came on five years before death. Intelligence was normal throughout. The duration of the illness was 24 years. The brain and cord were microscopically examined by Weir Mitchell, who found typical disseminated sclerosis. The patches were only in the cord, and chiefly affected the cervical and dorsal regions.

Other cases of disseminated sclerosis appearing under the type of a chronic myelitis are related by Siemens,[2] Schultze,[3] Zacher,[4] and Greiff.[5]

Disseminated sclerosis may be present under the guise of **ataxic paraplegia**. I am in possession of the following unpublished case which was considered throughout its course to be an example of ataxic paraplegia.

Case VII.—H. R., 35, an unmarried woman, came under observation on November 12, 1887.

Her previous history was unimportant. No history of acute illness, rheumatism, or syphilis. The present illness commenced with gradual failure of vision in the left eye about nine months previously. Later, weakness and unsteadiness began to appear in the lower limbs.

*Present State* (November 12).—The patient is an emotional but intelligent woman. The upper limbs are normal. In the lower extremities the knee-jerks are both exaggerated, and ankle-clonus is present on both sides. Plantar reflexes increased. There is very slight rigidity of the legs. The patient walks very unsteadily, throws the legs forward in a jerky manner, bringing the feet down suddenly. She falls when standing with the eyes closed and the feet together. Sensation is

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[1] *American Journal of the Medical Sciences*, 1868, Vol. II., p. 138.

[2] *Archiv für Psychiatrie*, X., p. 135.

[3] *Ibid.* XI., p. 216.

[4] *Ibid.* XIII., p. 168.

[5] *Ibid.* XIV., p. 287.

normal, and there is no pain anywhere. Slight tremor of the lips observed at times, but there is not the slightest sign of tremor elsewhere. Speech normal. Disseminated choroiditis and optic atrophy very marked in the left eye. The refraction of that eye shows only a very low degree of myopia. No nystagmus. No paralysis of facial, ocular, or tongue muscles. No bladder or rectal symptoms.

December 24.—Retention of urine has suddenly come on. The walking has been more unsteady. A boil has formed over the left ischial tuberosity, and a carbuncle has made its appearance in the gluteal region.

December 31.—The urine has become alkaline, and contains pus, much mucus, and a little blood. In both lumbar regions a very movable mass could be detected readily on palpation, combined with deep inspiration. A bedsore has formed over the sacrum. There is no anæsthesia, and the patient can move her legs fairly well.

January 7, 1888.—A violent attack of sickness and diarrhœa came on, the temperature rushed up to 104°. She rapidly became comatose, and died.

At the *autopsy* both kidneys were found to be very movable, and to be riddled with large multiple abscesses.

The foramen magnum was so small as to barely admit the middle finger. The narrowing of this opening was caused by a greatly enlarged odontoid process extending through the foramen, so as to make the latter reniform with the concavity forwards. No constriction of the cord was found. To the naked eye the brain and spinal cord, viewed externally and on section, appeared normal. Sections through the cord, examined microscopically, however, revealed the undoubted presence of disseminated sclerosis. From several of these sections I have made the accompanying drawings (Figs. 7, 8, 9). The brain, unfortunately, was never examined microscopically.

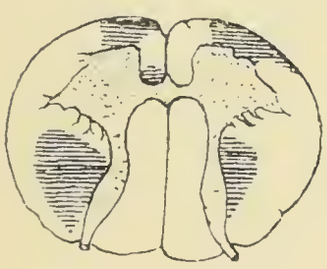

FIG 7.

CERVICAL. × 2.

FIG.8

DORSAL. × 2.

FIG.9

LUMBAR. × 2.

CASE VII.—The above drawings were made from sections stained with aniline blue black. The shading indicates the sclerotic patches.

The following anomalous case, published by De Fleury,[1] is also a fairly good example of the ataxic paraplegic type. In ataxic paraplegia, however, "lightning pains" are almost always absent.

A man aged 19 began in 1882 with pains of a "lightning" character in the legs. Progressive enfeeblement of the legs. Permanent contractures. Exaggerated knee-jerks and very marked ankle-clonus. Standing upright is difficult and the walk is hesitating. Rhomberg's symptom. Trophic changes in the nails of the great toes. Sensation normal. No nystagmus. No trembling of the limbs or of the voice. Death followed an apoplectiform attack in 1883. At the autopsy no patches were found in the brain, but there were several sclerotic patches scattered in the medulla and cord.

The **tabetic type** of disseminated sclerosis is sometimes met with. In these cases the posterior columns are largely involved.

Bourneville[2] quotes the following case: Josephine L., 46, has been suffering for two years. She presented the following ataxic symptoms—difficulty of walking with closed eyes; notion of position with respect to lower limbs greatly lost; frequent "lightning pains" in the knees and legs; girdle pains. But along with these were noted: considerable paralytic enfeeblement of the lower limbs; preservation of the different kinds of sensibility in the upper and lower extremities; vision normal. The woman succumbed to pyelo-nephritis, complicated with sacral bedsores. At the autopsy patches of sclerosis were seen in the left sixth cranial nerve, both optic nerves, pons, right crus on the surface of the lateral ventricles, in the centrum ovale, and medulla. In the spinal cord there were several large patches in the posterior columns, and many smaller ones implicating the anterior and lateral columns.

The case of Josephine Paget, reported by Cruveihlier,[3] is another example of this type.

Bourneville[4] reports another case. The patient was a woman

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[1] *Loc. cit.*

[2] Charcot's "Lectures on the Nervous System," *New Sydenham Society*, 1877, p. 199.

[3] "Anatomie Pathologique," 1835-1842, Liv. XXXVIII., Pl. 5.

[4] "Nouvelle étude sur quelques points de la sclérose en plaques disséminées," Paris, 1869, Chap. II., Obs. xxi.

named Broisat, and the most prominent symptoms were "lightning" pains and impaired sensibility.

Occasionally cases are recorded in which symptoms and lesions of *tabes dorsalis and disseminated sclerosis co-exist.* The legs may present the symptoms of tabes, while in the arms there may be the jerky inco-ordination of disseminated sclerosis. Such combinations must be purely accidental, as the former disease is mainly syphilitic in origin, while the latter seems to be seldom, if ever, the result of syphilis. Two cases under the care of Friedreich are related in detail by Bourneville[1] as examples of the co-existence of the two diseases. The first was a woman of 35, in whom feebleness of the right leg began at 16. Then feebleness of the left leg, "lightning pains," weakness of the right arm, then of the left at 20 years; speech embarrassed and somewhat unintelligible, with convulsive attacks in the lower limbs at 30 years. On admission the following were noticed: Vertigo, spasmodic contracture of the legs, embarrassment of speech, trembling of the head and neck, nystagmus, ataxic movements especially seen in the gait; typhoid fever; death. The brain showed no sclerotic areas. In the cord chiefly the posterior and lateral columns were affected irregularly, but the anterior columns and grey matter at certain parts also contained patches of sclerosis. Friedreich's second case was a woman, aged 32. The disease began at 17 with weakness and lancinating pains in the lower extremities. At 26 weakness appeared in the upper limbs. On admission the speech was stammering, slight nystagmus, frontal pains, intention tremor in arms, marked ataxia in the movements, and inability to stand without support. Finally there was œdema of lungs, albuminuria, diarrhœa, and death. The posterior columns were extremely diseased, and patches of sclerosis were found in other parts of the central nervous system.

Bourneville[2] relates also the case of Josephine C., which during life presented combined symptoms of disseminated sclerosis and locomotor ataxia. After death the posterior columns

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[1] *Ibid.*, Obs. xxi.

[2] Charcot's "Lectures on Diseases of the Nervous System," *New Sydenham Society*, 1877, p. 214.

were found sclerosed nearly throughout their extent, and there were many sclerotic patches in other situations.

**Hysterical Type.**—Disseminated sclerosis not unfrequently lies hidden under the cloak of hysteria. In a considerable number of cases, especially in women, the earlier symptoms are very apt to be thought hysterical. In Case VI., for a long time, the question whether hysteria could be excluded came in for serious consideration. In a few cases, however, symptoms apparently of a neurotic character have alone shown themselves throughout the disease. This is well seen in the following case, published by Buzzard[1] :—

The patient was a woman, aged 25, who for the last twenty years had been subject to attacks of vomiting, without nausea, after nearly every meal, and also to aching of the legs. Eight years ago she lost her voice for two months. Four and a half years ago the aching got worse, and attacks of shooting pains in the head and neck appeared. At this time also the toes became tender, but the tenderness disappeared after two months. Twelve months ago the legs began to get stiff, and on two occasions during the last fifteen months the urine had to be drawn off. On admission, there was no tremor, no nystagmus, no alteration in the speech. Her manner is highly hysterical. The grasp of both hands is good. She complains of a feeling of tightness round the waist, "pins and needles" in the fingers, and other sensory phenomena. Sensation is normal in the arms, but tactile and painful sensibility is much impaired all over the legs and thighs. The knee-jerks were well marked, but ankle-clonus could not be obtained because of very considerable rigidity in the legs. Plantar reflex present on both sides; wrist-jerks not increased. Dr. Buzzard states that for a long time he distinctly inclined to the belief that the case was of functional character. At the autopsy soon after—at Guy's Hospital—patches of sclerosis were found in the pons, medulla, and cord. In the lumbar enlargement, the whole transverse area, including the grey matter, was affected.

Another series of anomalous cases occur under what might be called the **paralytic** form of disseminated sclerosis. This

[1] "Simulation of Hysteria by Organic Disease," London, 1891, p. 89.

presents several varieties according to the extent and the seat of the motor troubles. Sometimes the paralysis invades successively the legs, arms, a part of the face, one or more muscles of the orbit, and tends to generalisation. Sometimes it remains limited to certain parts of the body, and takes on the characters of monoplegia, paraplegia, or hemiplegia. In addition, a limb may be only partially or may be completely affected, and sometimes the condition of pure hemiplegia is changed by the generalisation of the paralytic phenomena and the appearance of cerebral troubles. One usually finds that there is agreement between the seat of the patches and the localisation of the motor troubles.

Hemiplegia usually develops gradually, the paralysis attacking one limb before occupying one side of the body. In one of the following cases reported by Vulpian, however, we have a unique example of a sudden onset. The hemiplegia may remain in the part first attacked for a long or short time, constituting a monoplegia. Hemianæsthesia rarely accompanies the hemiplegia, but was seen in two of the following cases. There are two principal forms of hemiplegia met with, viz.: (1) partial and confined to the limbs, (2) total and invading at the same time the limbs and face.

Gilbert and Lion[1] quote a good example of the *partial hemiplegia*, which is the least frequent. The patient was a woman of 63, in whom weakness of the right leg appeared; this gradually increased, but remained limited to that limb for five years. Following this monoplegia the arm of the same side was attacked, and for the next five years the motor troubles persisted and progressively increased. On admission ten years after the appearance of the first symptom there was almost complete paralysis of the lower limb; the hand and forearm were affected, but the upper arm and shoulder escaped. These motor troubles were accompanied by abolition of sensibility, incomplete in the leg and thigh, but complete at the level of the hand and wrist. Bedsores; death. The autopsy showed disseminated sclerosis, and the chief patches were found in the right and left lateral columns and the left posterior horn and column in the cervical region. The dorsal and lumbar regions

[1] *Archiv. de Physiol. Norm. et Path.*, Paris, 1887, S. 3, X., p. 126.

showed no patches, and there were no sclerotic foci in the cerebral hemispheres, cerebellum, crura, pons, or medulla.

Werner[1] relates a very similar case in a man of 59. Here the left arm and the left leg were affected, and sclerotic patches were discovered in the left half of the cervical and lumbar regions of the cord. Other patches were in the pons and the white substance of the brain.

Babiniski[2] relates a case, which is a sort of transition form between the partial and total hemiplegia. In a patient, aged 18, the paralysis started first in the left lower limb, then rapidly invaded the upper limb of the same side, but remained three weeks before attacking the face. Speech was embarrassed. Patches were seen on the surface of the pons, medulla, and in the interior of the cord. The crossed pyramidal tract was affected on the left in the cervical, dorsal, and lumbar regions; on the right, in the lumbar region only.

Cases of *total hemiplegia* have been more frequently observed. Guttmann[3] publishes the case of a woman of 47, in whom there was paresis of the left leg and arm, and paralysis of the left side of the face and left half of the tongue, together with complete anæsthesia of the left side of the body, including abolition of taste, smell, and hearing on the left side. In addition, there was complete paralysis of the left external rectus and syllabic speech. The autopsy showed extensive disseminated sclerosis, especially in the region of the fourth ventricle.

Another case is related by Vulpian.[4] In a woman of 43, there was sudden paralysis of the right side of the face; this remained isolated for six months, and then total hemiplegia supervened. She had three attacks of hemiplegia, the last two with aphasia. The sudden onset of severe vertigo and aphasia looked very like a cerebral lesion, but patches were only found upon the pons and in the middle of the right cerebellar peduncle and the medulla. Large patches also were seen in the right antero-lateral tract of the cervical region of the cord.

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[1] *Fortschrifte der Medicin*, Bd. I., 1883.

[2] "Étude Anatomique et Clinique sur la Sclérose en Plaques."—*Thèse de Paris*, 1885, p. 75.

[3] *Berliner Zeitschrift für klinische Medicin*, 1880, Bd. II., S. 46.

[4] *Union Médicale*, 1866, p. 507.

Jolly[1] gives a good example in a woman of paralysis beginning in the leg, then rapidly invading the arm, then the face, and two months later becoming general. There were patches in the medullary subs tance of the brain, at the periphery of the lateral ventricles, and posterior parts of lateral columns.

In a case by Marie,[2] also, the invasion of the face was the signal for the generalisation of the paralytic phenomena.

In very rare instances disseminated sclerosis has presented the clinical features of **general paralysis of the insane.** In a case of this kind reported by Mickle,[3] the autopsy showed, in addition to the characteristic lesions of general paralysis, patches of sclerosis disseminated here and there throughout the nervous tissues. Claus[4] relates a case with symptoms closely resembling those of general paralysis of the insane, at the autopsy of which typical disseminated sclerosis was found. Cases constituting veritable connecting links between the two affections have been published by Charcot,[5] Zacher,[6] and Spitzka.[7]

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[1] *Archiv f. Psychiatrie*, Bd. III., S. 211.

[2] *Thèse Babiniski*, p. 90.

[3] "General Paralysis of the Insane." London, Second Edition, p. 231.

[4] *Brain*, Vol. II., 1879, p. 142.

[5] *La Semaine Médicale*, Paris, January 27, 1892.

[6] *Archiv f. Psychiatrie*, XIII., p. 168.

[7] *Journal of Nervous and Mental Diseases*, 1877. Also "Insanity, its Classification, Diagnosis, and Treatment."

## CHAPTER IV.

### DIAGNOSIS OF DISSEMINATED SCLEROSIS.

THERE are few nervous diseases more easily recognised than disseminated sclerosis when typically developed, there are few which present so much difficulty when the symptoms which constitute the type are almost all absent or but faintly expressed. It is in perfect harmony with the irregular location of the disease, and the lack of any constant rule governing the distribution of the sclerotic foci, that there is no constant clinical picture by which its existence can be accurately determined in all cases.

I propose first to consider the differential diagnosis of disseminated sclerosis from *hysteria*. Disseminated sclerosis is not unfrequently mistaken in its early stages for the latter disease, especially when it occurs in young adult females soon after some moral shock or long-continued mental strain. Again, a considerable number of typical cases of disseminated sclerosis in women and even in men display hysterical symptoms. Also in the history of a case of disseminated sclerosis one frequently notices various subjective sensations, more or less sudden loss of power, or stiffness in one or other limb, or loss of sight; these may clear off and not reappear for a long time, or may fly from one part of the body to another—all this is quite consistent with hysteria. Tremor, again, is often observed in hysteria, and may in both diseases follow injury. From the practical standpoint the recognition of organic from hysterical tremor due to trauma is of the utmost importance. Accidents by rail and by machinery have become so common, and, in consequence, litigation over damages is so frequent, that every subject connected with such accidents is bound to be tested with the most rigid scrutiny. The subject is one of peculiar difficulty. In both diseases the tremor is rendered worse by emotional excitement, and under the gaze of bystanders. The tremor of disseminated sclerosis may also, under the influence of great excitement, persist during repose, and in hysteria there is often noticed a clumsiness of movement of the hand when directed towards an

object, somewhat like the movement seen in disseminated sclerosis. At other times, however, if an hysterical patient is asked to touch an object with her finger she does so without difficulty or hesitation, but when the finger has rested upon the object for two or three seconds the arm becomes affected by somewhat rude tremors—this is in striking contrast to the same act in disseminated sclerosis. Again, in hysteria the tremor is of a much finer character, and there is an absence of actual inco-ordination. Stammering and loss of articulation are the usual speech troubles of hysteria, while nystagmus is absolute evidence of more than hysteria. Incontinence of urine is almost unknown in hysteria, though retention is common. Again, a uniform persistent ankle-clonus is extremely rare in hysteria, but occasionally a spurious clonus may be obtained in that disease. Buzzard[1] attaches great diagnostic importance to the behaviour of the plantar reflex, holding that it is nearly always absent in hysterical paraplegia. He has also noted atrophy of the optic nerve in 46·6 per cent of the "hysterical type" of disseminated sclerosis. Visual troubles themselves are very frequently a fertile source of error. A girl may complain of more or less rapid loss of sight, the fundus is found to be normal, and taking into consideration a history of loss of power in a leg, numbness or coldness of a limb, and the like, she may be regarded as hysterical, and be assured that she will entirely recover, when really she is suffering from disseminated sclerosis. A localised atrophy of muscle with reaction of degeneration occurs sometimes in the course of disseminated sclerosis; the recognition of such a symptom would immediately exclude hysteria. On the other hand, considerable caution must be observed lest purely functional disease be diagnosed as disseminated sclerosis. Moxon[2] says that he has seen several patients about whom, for a long time, he had been in doubt, but who before long completely and permanently recovered. The following case illustrates well this difficulty of diagnosis:—

Case VIII.—Elizabeth H., 19, domestic servant, is an out-patient at the Manchester Royal Infirmary under the care of Dr. Bury.

Seven years ago she had a severe attack of rheumatic fever, which kept her in bed for two months. Six years ago the head and neck began

[1] "Simulation of Hysteria by Organic Disease," p. 98. London, 1891.

[2] *Loc. cit.*

shaking, and a week later her hands started trembling. These tremors were not constant. A month later tremor appeared in the legs, and this greatly interfered with walking. Soon after the whole body began to be tremulous. The tremor generally became worse when she was excited. Her speech became affected three years ago, and during the last two years she has had occasional diplopia. Her vision has been very imperfect this last twelve months. She has suffered much from vertigo of the gyratory variety, and tingling and numbness in the extremities have been often experienced. She has had frequent "fits" since the commencement of the present illness; these last about ten minutes, are preceded by the "globus hystericus" and partial loss of consciousness; profuse sweating, and complete freedom from injury are other features of the attacks. The bladder functions have been normal throughout. The family history is good, but the mother is decidedly hysterical.

*Present Condition* (October 10, 1894).—As she is seated in a chair all that can be seen is a very marked tremor of the head and neck. This becomes slightly less when the attention is withdrawn, and entirely ceases when the patient lies down. She puts out her hands before her without hesitation, and soon a coarse irregular tremor appears in both arms, but is more marked on the right. This tremor also disappears on rest. No tremor is to be seen in the trunk or legs. The gait is slightly ataxic, yet somewhat hesitating. She can easily stand with her eyes closed, and is able to touch the tip of her nose with a given finger. The grasp of the right hand is less powerful than that of the left. The movements of the legs are good. Both knee-jerks are exaggerated, and well-marked ankle-clonus is obtained on both sides. The wrist- and elbow-jerks are just present, but both plantar reflexes are absent. The speech is slow, monotonous, sometimes rather syllabic, but often slurring. There appears to be slight impairment of sensation on the ulnar side of the right hand and arm, otherwise the sensibility is normal. She complains of severe pains in the back of the neck and in the arms. No nystagmus, no strabismus, and no crossed amblyopia. Both optic discs look perfectly healthy. Other cranial nerves normal.

One of the nearest clinical allies of disseminated sclerosis is *Friedreich's disease.* Charcot and others for a long time thought that the cases of hereditary ataxia, described by Friedreich, were only cases of disseminated sclerosis in which the sclerosis was chiefly confined to the posterior columns. In common to both, we find imperfection of speech, nystagmus, and tremor, unassociated, as a rule, with sensory or trophic disorders. But these troubles are late manifestations in Friedreich's disease, and only appear long after the ataxy and loss of

knee-jerks. Moreover, symptoms of disseminated sclerosis not unfrequently begin at an earlier age than those of Friedreich's disease; inco-ordination is the main motor symptom in the one disease, tremor in the other; the gait, usually ataxic in Friedreich's disease, is spastic in disseminated sclerosis; the knee-jerks, absent in the former, are increased in the latter; nystagmus is much more frequently observed in disseminated sclerosis, and strabismus, while seen in about half the cases of disseminated sclerosis, is very rare in Friedreich's disease. Vertigo has been also noted as a symptom common to both, but is much less often present in Friedreich's disease. Convulsions occur in both, but in Friedreich's disease they are probably accidental coincidences. In 2 per cent of the cases of hereditary ataxia the knee-jerk is normal or even exaggerated, and, on the other hand, this reflex is occasionally lost in disseminated sclerosis. There is a pretty close resemblance between the speech of Friedreich's disease and that of disseminated sclerosis. According to Wyllie,[1] the characteristic speech of hereditary ataxia has in it almost always more or less of that "staccato" element which is so markedly present in the speech of disseminated sclerosis. But this element may not be very striking, and often the utterance is merely slow, thick, and drawling. Finally, apoplectiform seizures, vesical paralysis, mental disturbances, and frequent remissions in the course of the disease are invariably wanting in hereditary ataxia. Great difficulty, however, is experienced in the transitional or mixed forms of the diseases in forming a correct diagnosis. The following case is a good example of this difficulty:—

Case IX.—John W., aged 23, was admitted as an in-patient at the Manchester Royal Infirmary, under the care of Dr. Bury, on March 15, 1894.

At seven years old he had scarlet fever and measles, and a year later a very severe fall on the head. Very soon after this his mother noticed his walking was stumbling and shaking, and that he had incontinence of urine. Eleven years ago his speech became altered, his temper irritable, and the body generally began shaking. In June, 1884, he began to have attacks of shooting pain, starting in the left axilla and

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[1] *Edinburgh Med. Jour.*, Vol. XXXIX., April, 1894, p. 877.

going down both legs. He has had the girdle-sensation at times. Eight years ago his hands became unsteady, and for the last five years he has not been able to walk. There is no family history of nervous disease.

*Present State* (March 15, 1894).—The patient is fairly well grown, and has a stolid but pleasant expression. There is a condition of pes cavus in both feet, and the toes are hyperextended. A fine, jerky tremor affects the head, body, and arms when these parts are unsupported. If he stretches out his arms the oscillations become more marked, but the tremor is not increased by the act of drinking. Great difficulty is experienced in touching the tip of the nose with a given finger when the eyes are closed, because of the inco-ordination present. The considerable inco-ordination of the fingers is displayed in trying to pick up a pin from the floor, and he finds it difficult to write. There is marked lordosis. Slight horizontal nystagmus. The pupils react to light and accommodation, and the optic discs are normal. The speech is slow and slightly syllabic, and there is fine fibrillary tremor of the tongue. Both knee-jerks are absent, and there is no ankle-clonus. The superficial reflexes are present, but sluggish. The grasp of both hands is good, and the patient can feel and localise the touch of a pin's head all over the body, and can distinguish between the point and head of a pin. The muscular sense is normal. There is distinct reaction of degeneration obtained in the quadriceps, extensor longus digitorum and peronei of both legs: testing was difficult, because of the involuntary jerkings of the muscles. No paralysis of the facial, ocular, or tongue muscles. No affection of the bladder or rectum. No hemianopia and no colour-blindness. Memory and intelligence good.

April 14, 1894.—The patient has occasionally very violent tremors in his head, neck, and arms. He has great difficulty in keeping his head still. The movements of this part are chiefly lateral.

The diagnosis from *locomotor ataxia* is not as a rule difficult, except in those anomalous forms already mentioned. The main points of distinction are: locomotor ataxia is very rare in women, disseminated sclerosis is said to be about equal in the two sexes; locomotor ataxia seldom occurs before the twentieth year, disseminated sclerosis not unfrequently before this period; in the former affections of sensibility are early and constant, but in the latter they are generally absent; the Argyll-Robertson pupil is excessively rare in disseminated sclerosis, and nystagmus is equivalently so in locomotor ataxia; the knee-jerk and ankle-clonus are absent in locomotor ataxia, and

there are no rigidities, while rigidities, knee-jerks, and ankle-clonus are commonly present in disseminated sclerosis; speech affections, usually present in the latter, are absent as a rule in the former; in locomotor ataxia simple inco-ordination is met with in contradistinction to the intention tremor of disseminated sclerosis; and, finally, mental disturbance is rare in the former, frequent in the latter. I have recently had an opportunity of seeing a well-marked intention tremor in the right hand and arm of a tabetic patient under the care of Dr. Bury. The following case is interesting from a diagnostic point of view. The question arises whether it is a case of locomotor ataxia, or disseminated sclerosis, or a combination of the two diseases.

Case X.—Hugh F., aged 23, was admitted as an in-patient at the Manchester Royal Infirmary, under the care of Dr. Ross, on September 17, 1887.

In January, 1884, he experienced difficulty in passing urine. There was no pain, but he was unable to empty his bladder. In June of the same year he had diplopia, which lasted three months and then disappeared. The following September weakness appeared in the left leg, and there was a feeling of great weight in the left calf. After resting for a couple of months these improved. Early in 1885 the right leg became affected, and soon after the left leg became as bad as ever, and he had to get along on crutches. Later, again, he could dispense with these and walk without assistance, but with dragging of the right foot. Six months ago he experienced the girdle-sensation, and lately his speech has altered. No history of syphilis, rheumatism, or acute infectious disease. A sister is said to be paralysed, and an aunt was subject to "fits."

*Present Condition* (September 17, 1887).—Patient looks healthy. Has a somewhat vacant expression, but is fairly intelligent. No vertigo or headache. There is marked inco-ordination in the lower extremities, the gait is unsteady and ataxic, with slight dragging of the right foot, the heel rubbing the ground. He cannot stand with the feet together and the eyes closed, and stumbles in the dark. The legs can both be raised well from the bed, but they are allowed to drop suddenly. There is apparently some wasting of the muscles of both legs, but no reaction of degeneration is obtained. He has a fairly correct idea of the position of his legs in bed. On the outer aspect of the right leg and in both soles there is slight impairment of tactile sensation. He sometimes has painful spasmodic muscular contractions in the right leg. On holding out the hands marked tremor is noticed in both upper limbs, and this is rendered much worse by any

attempt to seize anything. When trying to drink from a mug, he spills the water. The task of picking up a pin is performed with great difficulty. The tremor ceases entirely on rest. There is some difficulty in touching the tip of the nose with the eyes open, but when the latter are closed this task is almost impossible at one attempt. Both knee-jerks are quite gone, and ankle-clonus, the wrist- and the elbow-jerks are not obtained. The plantar and abdominal reflexes are absent on both sides, but the left epigastric reflex is just obtained. There is now no evidence of strabismus, the eyeballs moving well in all directions. Slight impairment of vision in the left eye, but both fundi appear normal. No paralysis of the facial or tongue muscles. Hearing and smell are normal. The speech is slightly hesitating and drawling, but not syllabic. Considerable retention of urine, necessitating catheterism twice daily—there is no incontinence. The urine contains a very small quantity of albumen, and the microscope reveals a few pus cells.

*Paralysis Agitans* is a disease which by the older neurologists was frequently confused with disseminated sclerosis. The affections, however, differ very much from each other. The tremor of paralysis agitans is always more regular, more rhythmical, and of finer character. Occasionally, however, tremor is absent in both diseases, and, again, the tremor of paralysis agitans may in very early stages cease during rest. In disseminated sclerosis, the head is usually markedly tremulous; in paralysis agitans, tremor of the head is occasionally, but not commonly, seen. Nystagmus is unknown in the latter, and the articulation is quick, with a tendency to run the words together, quite the opposite to disseminated sclerosis. The facial aspect, the forward stoop, early rigidity, and the "cigarette-rolling" hands are peculiar to paralysis agitans. Disseminated sclerosis is generally a disease of youth, while paralysis agitans usually occurs in advanced life. Hadden,[1] however, records a case of paralysis agitans in a young man of 28, and Charcot, Duchenne, and Meschede all have seen examples of this disease in patients under 17 years of age. Finally, in paralysis agitans, paresis occurs long after the tremor, and bladder disturbance is wanting. In very rare instances, disseminated sclerosis has been found after death, although typical signs of paralysis agitans had been present during life, but these are probably accidental coincidences.

[1] *Brain*, XIII., 1890, p. 465

The following is most likely an early case of paralysis agitans, but has several points about it of diagnostic interest:—

Case XI.—Elizabeth B., 41, is an out-patient at the Manchester Royal Infirmary, under the care of Dr. Bury.

She was quite well up to her last confinement, five years ago. This was very difficult, instruments had to be used, and the perineum was badly ruptured. She was in bed for ten weeks following, and continued very weak for a long time. Two and a half years ago she underwent the operation of perineorrhaphy, and shortly afterwards she noticed she was very clumsy in using the thumb and index finger on the right side. Two years ago tremor and weakness developed in the right hand, and then in the right arm. Later similar tremor and weakness appeared in the right leg, then in the back, and finally in the left hand.

*Present Condition* (November 8, 1894).—The face is flushed, anxious, and the features look uniformly swollen and fixed. She has a slight forward stoop. There is in all probability some slight weakness on the right side of the face. The tongue is protruded straight. The right hand is slightly flexed at the wrist, the fingers are flexed at the metacarpo-phalangeal joints, and nearly fully extended at the inter-phalangeal joints, and the palmar surfaces of the thumb and index-finger are kept in close apposition. The movements of the right upper arm, especially those of extension, are weak. There is also marked weakness in all the muscles of the right forearm and fingers, and the patient finds it difficult to relax the grasp. The dynamometer records 38 on the right and 48 on the left. Shrugging of the right shoulder is less marked than that of the left, and the right deltoid is slightly weaker than the left. Some of the movements of the left upper arm are poor, but the left lower arm is fairly strong. There is some slight rigidity to passive movement in bending the right elbow, and also the right ankle. A well-marked rhythmical fairly coarse tremor is seen in the right upper and lower extremities, and also, though in a less marked degree, in the trunk muscles. In the left arm and leg, and also in the head and neck, a slight tremor is seen. The tremor does not quite cease on rest in the right arm, but the movements are then much quieter. The tremor in the other parts disappears on rest. The knee-jerks are both increased and about equal. Ankle-clonus is obtained on both sides, but is more marked on the right. The plantar reflexes and wrist-jerks are present. The elbow-jerk and the epigastric reflex are obtained only on the right side. The gait is fairly normal, and there is no disturbance of sensation. The vision is normal, and there is no nystagmus. The speech is inclined to be monotonous, but is not unduly rapid, nor is it syllabic. The bladder and rectum are normal. Patient complains of severe giddiness at times. No hysterical manifestation.

*General Paralysis of the Insane* and disseminated sclerosis are sometimes indistinguishable during life. When it is borne in mind that the patient afflicted with disseminated sclerosis exhibits tremor and speech disturbance in addition to his mental trouble, it will be understood that, with some modification of the typical signs, the case may simulate one of paretic dementia, and there are cases in which it is exceeding difficult to decide whether they belong to an aberrant type of disseminated sclerosis or to the sclerotic type of paretic dementia. Cases of disseminated sclerosis, in which the mental symptoms resembled those found in general paralysis of the insane, have been reported by Jaccoud,[1] Leube,[2] Liouville,[3] Valentiner,[4] and others. According to Wyllie[5] an element of "staccato" utterance is often present in the speech of general paralysis. Charcot[6] also emphasises the resemblance of the speech in these two diseases. He says: "I even believe that in a good many cases, apart from the help obtained from the consideration of accompanying phenomena, the distinction would be almost impossible. And that the resemblance may be still closer, owing to the circumstance that in multiple sclerosis, as in general paralysis of the insane, emission of words is sometimes preceded or accompanied—as you may remark in our patient—by a slight, as it were, convulsive contraction of the lips." Kussmaul,[7] however, holds that syllable stumbling, the most characteristic of all the features in the speech of general paralysis, never occurs in disseminated sclerosis. In general paralysis he says: "Both articulate sounds and syllables are misplaced and thrown into confusion. To borrow Westphal's admirable illustration, the general paralytic in trying to say 'artillery' calls it 'artrallerary'; the patient with insular sclerosis, on the other hand, pronounces it 'ar-til-ler-y.'" The tremulous movements of the general paralytic are developed only on exertion, and consist in twitching contractions of the muscles, which may disorder voluntary movements in a manner not altogether unlike that of disseminated

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[1] *Loc. cit.* [2] *Loc. cit.* [3] *Loc. cit.*

[4] *Loc. cit.* [5] *Loc. cit.*

[6] "Leçons sur les Maladies du Système Nerveux," 1875, p. 236.

[7] *Ziemssen's Cyclopædia of Pract. Med.*, American Edition, XIV., p. 664.

sclerosis. In both diseases there are usually exaggerated reflexes, and apoplectiform attacks occur in both. Inequality of the pupils and absence of iris reflex, which are common features of general paralysis, are rare in disseminated sclerosis. Diagnostic difficulty is especially marked in early stages, as is seen in the case briefly stated below:—

Case XII.—Sarah B., 38, is an out-patient at the Manchester Royal Infirmary under the care of Dr. Bury.

The present illness began twelve months ago with weakness in the right hand and arm, and during the last seven months her speech has altered. Her previous health had been good. No history of syphilis, and there is no family history of importance.

*Present Condition* (October 24, 1894).—Both palpebral fissures are wide, giving a staring aspect. When questioned she is rather stupid in her answers. The speech is monotonous and typically syllabic. There is slight weakness in the grasp of the right hand. On movement slight tremor is brought out in the right arm, but this disappears entirely on rest. The tremor is slightly less marked when the attention is withdrawn. The knee-, wrist-, and elbow-jerks are all exaggerated, ankle-clonus is obtained on both sides and both plantar reflexes are present. The patient states that her speech goes at times and she can only speak in a whisper. There is very marked tremor of the tongue. No vertigo, no nystagmus, and the vision is good. The left pupil is distinctly less than the right, and the iris reacts very slowly to light and to accommodation on both sides. She walks with slow, short, shuffling steps. There appears to be some impairment of sensation on the ulnar side of both arms. She has no delusions, but of late her memory for recent events has been very bad. Her sister also informed me that the patient readily flies into a temper and is perpetually irritable, a condition quite different from that seen a year ago.

The diagnosis of disseminated sclerosis in children is difficult because of the age rather than the peculiar characters of the disease. But in children we have the advantage of being able to exclude senile trembling and paralysis agitans, which have to be considered in cases much older; on the other hand there is the disadvantage, as we have already seen, of taking Friedreich's disease into consideration. In children again, besides hereditary ataxia, *birth palsies* are sometimes a source of difficulty. A history of protracted or instrumental labour fol-

lowed by semi-asphyxia, or convulsions, for a few days in a first-born child, would of course be a considerable aid to diagnosis, but such history cannot always be ascertained. In addition the parents very often notice nothing abnormal until the child reaches its second or third year, and accordingly date the onset of the affection to that period. The following case shows a paralytic gait, nystagmus, syllabic speech, successive slow movements of flexion and extension in the fingers of the right hand, and an emotional and somewhat stupid mental condition. There is also a history of epileptiform seizures:—

Case XIII.—Margaret C., 12½, is an out-patient at the Manchester Royal Infirmary, under the care of Dr. Bury.

The mother tells me that her daughter was a seven months' child. The labour was somewhat prolonged, but no forceps were used. However, the child was "blue" for four days after birth, and she had several convulsive attacks. The patient has two brothers and one sister older than herself, who are perfectly healthy. The mother's first intimation that anything was wrong was when the child was two years old, and then she found that her daughter could not walk at all—all her other children could at that age. She also noticed that the patient did not take the same notice of things as other babies of the same age. Walking did not begin until seven years, and then the gait was very imperfect. She did not commence to speak until about the same time. Convulsions have occurred frequently.

*Present State* (November 9, 1894).—The child is very small for her age, has a somewhat stupid look, and is not very intelligent. She is very emotional, bursting out laughing or crying on slight cause. The memory is very poor. She can read short words, and after previously spelling them several times can pronounce some of the longer ones. She speaks rather indistinctly, pronouncing the words badly, with some hesitation between each syllable. The grasp of both hands is good. The muscles of the upper extremities are fairly strong, and there is no atrophy; the same applies to the lower limbs. On walking, the child drags her left leg very much, holding it stiff at the knee at the same time. A similar, but less marked, condition is noticed in the other leg. Both knee-jerks are increased, and ankle-clonus is just present on both sides. The plantar, abdominal, and epigastric reflexes are also obtained, but the wrist and elbow jerks appear to be absent. There is no affection of the facial muscles. Nystagmus is seen on lateral movements, and there is a left internal spasmodic strabismus. The tongue, on protrusion, is very unsteady, the tip

performing numerous irregular movements. Constant athetoid movements are noticed in the fingers of the right hands. She can, however, touch the tip of her nose fairly correctly with one of these fingers, even when the eyes are closed. The child passes urine into the bed nearly every night, but has complete control over the rectum.

Similarly *hereditary syphilis* in children has frequently been known to cause a spastic condition of the limbs, with "fits" and impaired intellect. The diagnosis is easily made from the peculiar physiognomy of congenital syphilis.

Again, *infantile hemiplegia* has sometimes to be excluded. It is not in its common and well-marked form that this affection is liable to be taken for disseminated sclerosis; it is rather in its obliterated forms, where there is only an awkwardness and not a complete paralysis, or, above all, when it is accompanied by hemichorea or athetosis. But an examination of the movements would show that they are produced in complete repose; they are irregular, without rhythm, and in the case of athetosis occupying the fingers and the toes. Again, the movements in athetosis are so characteristic that once seen they are never forgotten. The more the hemiplegic character is in evidence the easier is the distinction between the two diseases, and the occasional coincidence of hemianæsthesia would still further assure the diagnosis. Osler[1] has called attention to the difficulty attending a differential diagnosis in some of these cases, and quotes two cases illustrating this difficulty.

In adults *post-hemiplegic chorea* or athetosis, with the syllabic speech occasionally met with in aphasia, together with spastic gait and muscular weakness, could only at first sight resemble disseminated sclerosis. The history and associated conditions would rapidly dispel any further thought of this disease.

*Intracranial tumours* not unfrequently produce symptoms closely resembling those of disseminated sclerosis. Case II is a good example of this resemblance. When I first saw this patient there was absolutely typical intention tremor of the right arm, weakness in the right arm and leg, and an ataxic gait. This first made one think of disseminated sclerosis. On

[1] "Cerebral Palsies of Children," 1889, p. 66.

my second visit, however, undoubted optic neuritis was found; and I also had an opportunity of seeing him in one of those curious attacks of tetanoid rigidity. My diagnosis then became one of tumour in the left or middle lobe of the cerebellum pressing upon the left side of the pons, and I thought from a consideration of the history that the tumour very probably was a gummatous or tubercular deposit. At the autopsy I found a tubercular growth in the left optic thalamus. Tumours of the crus, cerebellum, pons, etc., have also produced similar tremor; but, as in tumour generally, this seems to be always unilateral. In cerebellar tumour, again, the often present nystagmus would still further increase the likeness between the two diseases, and a reeling gait exactly like that so often seen in cerebellar tumour was noticed in one of my cases of disseminated sclerosis. Convulsive attacks may appear in both, and headache and vomiting are not always prominent features of intracranial tumours. Optic neuritis, however, rarely occurs in disseminated sclerosis.

That the symptoms of genuine disseminated sclerosis may be closely simulated by conditions depending apparently on purely functional disturbances is well established. Westphal [1] has given the name of *pseudo-sclerosis* to this neurosis. He reports with great fulness two cases which presented typical symptoms of disseminated sclerosis (excepting nystagmus). Careful post-mortem examinations failed to reveal the slightest lesion of the central nervous system or peripheral nerves. Another case of this nature is related by Maguire.[2] Nystagmus was here again absent. A curious feature in Maguire's case and in Westphal's second case was that the movements of the eyes were very slow and performed with difficulty. Dawson-Williams[3] records the case of a girl of three and a half years old, in which symptoms closely corresponding to disseminated sclerosis followed an ordinary attack of measles. The patient is now ten years old, and still shows intention tremor in the head and all the limbs, and a spastic gait; but the syllabic speech seen earlier in the affection has now disappeared, and

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[1] *Archiv f. Psychiatrie*, Bd. XIV., 1883, p. 87.

[2] *Brain*, XI., April, 1888, p. 71.

[3] *Loc. cit.*

nystagmus has never been observed at any period. Foxwell[1] reports a case of rheumatic hyperpyrexia (temperature 111° F.) with nervous sequelæ, simulating disseminated sclerosis. Nystagmus was here again absent, but the other symptoms did not pass off during the whole time the man was under observation. Other examples are published by Langer,[2] Boinet and Salebert,[3] and similar cases have also been seen following diphtheria. Gowers[4] thinks that most of these cases have been examples of general paralysis of the insane. It seems to me that some are possibly hysterical, especially as nystagmus, which indicates an organic lesion, has been so often absent. In Maguire's case cerebral syphilis was not sufficiently excluded. Up to the present time, however, as far as I am aware, there have been no cases of pseudo-sclerosis in which optic atrophy has been noted. Optic atrophy being so frequent in disseminated sclerosis must, therefore, be of great diagnostic value when present.

Many cases of disseminated sclerosis present in their earlier stages the clinical features of *primary lateral sclerosis.* Charcot[5] and Oppenheim[6] both call attention to the fact that spastic paralysis should always excite a suspicion of disseminated sclerosis. I have already related examples of the disease, where a condition of spastic paraplegia had been the only symptom during life. Needless to say, in such cases the diagnosis is exceedingly difficult. An association of some eye-symptom, some disturbance of sensibility, or some psychical disorder, together with the spastic paraplegia, would be of great diagnostic value, and, however slight, should be carefully considered. Oppenheim,[7] Bruns,[8] and Zimmermann[9] assert that primary spastic paraplegia, together with a simultaneous affection of the optic nerve, is not an unfrequent clinical form of

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[1] *Loc. cit.*
[2] *Wien. med. Presse.*, 1884, p. 698.
[3] *Loc. cit.*
[4] *Loc. cit.*, p. 518.
[5] *Jour. de Méd. et de Chir.*, 1887.
[6] *Berl. klin. Woch.*, 1887, p. 904.
[7] *Ibid.*
[8] *Berlin klin. Woch.*, 1888, p. 90.
[9] *Loc. cit.*

disseminated sclerosis. Gowers,[1] Petersen,[2] and others speak of the rarity of ocular disturbances in primary lateral sclerosis. Gowers has only once seen optic nerve atrophy in an uncomplicated case of primary lateral sclerosis, and only a few isolated examples are to be met with in medical literature. Gnauck[3] mentions five cases of primary spastic paraplegia in which ocular disturbances never occurred. Very slight sensory derangements are occasionally present in primary lateral sclerosis; but marked sensory symptoms, though not common in disseminated sclerosis, are never present in pure lateral sclerosis. Alteration of speech in any form is not often met with in the latter, and, if present, would favour the diagnosis of disseminated sclerosis.

*Alcoholic Peripheral Neuritis* sometimes has to be considered in the differential diagnosis, for in this disease there is frequently tremor, and there may frequently be inco-ordination. The tremor of alcoholism usually occurs only on movement, and is irregular and considerable in range; it is most conspicuous in the arms, face, and tongue, but is to be seen also in the legs when these are put into voluntary motion, especially if the patient attempts to stand. Hadden[4] has drawn attention to the occasional occurrence of nystagmus in multiple neuritis due to alcohol. This observation is an important one, as the ataxy gives sometimes a *primâ facie* resemblance to disseminated sclerosis, which the presence of nystagmus would be liable to support. The diagnosis is usually readily made from the history and from concomitant signs of alcoholic abuse.

The diagnosis from *chronic mercurial poisoning* is rarely difficult. Charcot[5] says that the tremors of mercurial poisoning and of disseminated sclerosis are the same, but Gowers[6] asserts that in disseminated sclerosis the movements are wider in range and wilder in their irregularity. The speech is often affected in mercurial poisoning; there is also impairment of muscular power, and psychical disturbance is common. However, in dis-

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[1] "Medical Ophthalmoscopy," London, 1890, p. 195.

[2] *Centralblatt für prakt. Augenheilkunde*, 1886, p. 106.

[3] *Loc. cit.*

[4] Buzzard's "Paralysis from Peripheral Neuritis." London, 1886, p. 89.

[5] "Diseases of the Nervous System."—*New Sydenham Society*, 1877, Lecture VII., p. 188.

[6] "Diseases of the Nervous System, II., 1886, p. 889.

seminated sclerosis there is never the peculiar tremulous stammering which occurs in mercurial poisoning, and the presence of stomatitis, together with a history of working with the metal, soon shows the true nature of the case. At the present day, also, mercurial poisoning is met with only quite exceptionally.

*Chorea Minor* seldom causes any trouble in the differential diagnosis. The disorderly movements of chorea markedly differ from those seen in disseminated sclerosis, and in the former they persist when the limbs are at rest. Occasionally it happens, however, that choreiform movements complicate those proper to disseminated sclerosis.

*Syringomyelia* does not usually simulate disseminated sclerosis, but both diseases present great variety of symptoms. In syringomyelia disorders of motion of the lower extremities are frequent. These consist either of paraplegia, rarely complete and of the spasmodic kind, or of inco-ordination of the lower limbs. A peculiar shaking or trembling is sometimes observed in syringomyelia, and in both trophic disorders occur. According to Charcot there may be nystagmus in syringomyelia. Schultze has noted amaurosis, and finally bladder and rectal troubles are occasionally present in this disease. However, in syringomyelia the disorders of motion in the legs are only secondary, and, as the cervical enlargement is usually the original seat of the disease, one finds associated with the spastic paraplegia atrophy of the muscles supplied by the ulnar nerve. The "radial-tabetic" variety rarely has to be considered. As regards the trophic disturbances, the muscular atrophy occurs early and affects the arms in syringomyelia, late and attacking usually the legs in disseminated sclerosis; moreover, the trophic affections of the skin, nails, subcutaneous tissue, vessels, bones, etc., usually present in syringomyelia would be most exceptional in disseminated sclerosis. Again, sensory disturbances—excluding the subjective disorders of the early stages—are rarely met with in disseminated sclerosis except towards the conclusion of the disease. In syringomyelia sensibility to touch often persists, while analgesia or hyperalgesia with thermo-anæsthesia or hyperæsthesia are nearly always present in that disease. If bladder and rectal troubles are present in syringomyelia they are due to interference with the nutrition of these parts rather than to disturbances of the vesico-spinal centre.

If a patient were first seen in one of the apoplectiform seizures of disseminated sclerosis, a diagnosis of *true cerebral apoplexy* would probably be made, unless a clear previous history of symptoms pointing to disseminated sclerosis were given, and the clinical thermometer applied. If the apoplectiform attack were the first symptom of importance, as occasionally happens, the temperature would then be our only guide. This latter is markedly raised in the attacks seen in disseminated sclerosis, while in true apoplexy, at least for the first twenty-four hours, the temperature remains below the normal. As previously seen, it occasionally happens also that disseminated sclerosis is the reason for a slowly developing or even sudden hemiplegia, which may be falsely regarded as cerebral, whereas the autopsy shows several patches in the corresponding side of the cord.

*Acute Disseminated Myelitis* is not very likely to be mistaken for disseminated sclerosis, as the former is very rare, runs a much more rapid course, and does not present any of the classical symptoms of sclerotic disease. In both, however, as Dr. Dreschfeld[1] has recently stated, the optic nerve is frequently implicated, and both show amelioration of symptoms. *Chronic disseminated myelitis* is indistinguishable during life from the "spastic paraplegic type" of disseminated sclerosis.

*Chronic Bulbar Paralysis* has only very seldom to be considered. Disseminated sclerosis involving the medulla is seldom so symmetrical as to give rise to real difficulty, and there are practically always indications in other parts of the morbid process.

Among other diseases that have simulated disseminated sclerosis is *chronic lepto-meningitis cerebri.* In an example of the disease published by Gray[2] all the characteristic criteria of disseminated sclerosis were present. Happily such cases are very rare.

*Senile Tremor* is of fine character and occurs chiefly in extreme old age.

Finally, according to Charcot,[3] tremulous movements, indistinguishable from those of disseminated sclerosis, may be present in "chronic cervical meningitis with cortical sclerosis."

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[1] *Brit. Med. Jour.*, June 2, 1894, p. 1174. [2] *Loc. cit.*

[3] "Diseases of the Nervous System," *New Sydenham Society*, 1877, Lecture VII., p. 188.

## CHAPTER V.

### MORBID ANATOMY AND PATHOGENESIS OF DISSEMINATED SCLEROSIS.

THE pathological conditions of disseminated sclerosis are practically the same at all ages. The disease, according to most writers, consists of an overgrowth of the connective tissue of the brain and spinal cord, which has the characteristic peculiarity of being limited to spots or patches distributed in the most erratic fashion in almost any portion of the central nervous system.

Disseminated sclerosis is generally admitted to be one of the primary scleroses—the atrophy and degeneration of the nerve fibres in the patches are secondary to the interstitial changes—and the overgrowth of neuroglia is essentially the same as that of tabes dorsalis, primary lateral, and various other scleroses. That the process consists in an overgrowth of the connective tissue in the sclerosed areas has been, however, doubted by some. Popoff[1] believes that what most observers have looked upon as tracts of fibrous tissue lying between the nerve fibres are only degenerated products of the nerve fibres themselves. He considers that the methods of staining usually employed are unsuitable for studying the nature of the tissue. His method consists in first staining the sections in hæmatoxylin, then in a mixture of patent acid rubin, acetic acid and alcohol, and finally staining in orange. I tried his method in a considerable number of sections from my various cases, but entirely failed to agree with his opinion. His triple stain, far from disproving the fibrous nature of the tissue, brought out both the connective tissue and axis-cylinders remarkably well. Some specimens stained in the above way I subjected to pro-

[1] *Neurologisches Centralblatt*, No. IX., May 1, 1894.

longed teasing, which caused the individual fibrils of the connective tissue to stand out so clearly that there could be little doubt regarding their nature. The following drawing was made from one of these teased specimens:—

FIG. 10.

From a teased section through the dorsal region of Case VI., stained by Popoff's method. × 240.

Disseminated sclerosis has been found as an associated feature in some cases of congenital defect. Pollak[1] discovered disseminated sclerosis in an infant who had a defective corpus callosum, and exhibited the characteristic signs of the sclerotic affection side by side with the imbecility due to imperfect cerebral development. As previously noted, sclerotic patches have occurred conjointly with the characteristic lesions of general paralysis of the insane.

**Macroscopic Anatomy.**—The general aspect of the cerebro-spinal axis differs little from the normal. The sclerosis does not perceptibly affect the volume of the part. In advanced cases the cord frequently feels firmer than normal, as was seen in Case IV. As a rule, the morbid state is at once obvious in the fresh state to the naked eye. Bourneville[2] has, however, recorded one case which appeared to be healthy until the microscope was used, and in Case VII. the sclerotic patches in the cord were likewise only recognised histologically. In many other cases the patches are not very prominent, but are brought out much better after preservation in Müller's fluid. The older method of placing the specimens into alcohol, instead of further displaying the patches rendered them much less distinct. This

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[1] *Deutsches Arch. für klin. Med.*, Bd. XXIV., p. 404.

[2] *Mouvem. méd.*, 1868, No. 13.

may be another reason why disseminated sclerosis remained so long unknown. To the naked eye the sclerotic patches in the cord are very difficult to distinguish from disseminated myelitis. However, secondary degenerations, which are very rarely seen in disseminated sclerosis, usually occur in disseminated myelitis; and again, microscopic examination would show that, as a rule, in disseminated sclerosis the axis-cylinders persist in the patches, while the nerve fibres entirely disappear in disseminated myelitis. The myelitic areas also commonly have a slighter consistency, and are less sharply defined.

The *colour* of the sclerotic patches is usually greyish, but not unfrequently shows a yellowish or reddish tinge. They are a little darker and rather more translucent than the normal cortical grey matter of the brain. According to Charcot,[1] the fresh grey patches in the cord change to a salmon colour on exposure to the air. I could not, however, convince myself of this at the autopsy on Case VI. The colour of the nodules varies somewhat with their age.

*Relation to surrounding Healthy Tissue.*—Their cut surface in early stages may project above the surrounding healthy tissue; or, as is seen in most cases, occupy the same level; or, in advanced cases, retraction of the cut surface may take place. To the naked eye, the sclerotic areas are usually sharply defined against the sound tissue, but now and then a patch is surrounded by an ill-defined zone of a greyish-white appearance.

In *shape* they may be rounded or elliptical, but are often most irregular in outline. In the cord they are not infrequently wedge-shaped, extending inwards from the periphery, as seen in several of my drawings.

In *consistency* they are somewhat harder and denser than the normal tissue; sometimes extremely hard and almost leathery, and instances are recorded where the patches actually creaked under the knife; occasionally, also, in advanced cases they appear somewhat gelatinous, as seen in Case IV.; or they may be very soft and almost diffluent, as observed in Case XIV., and fluid may run from the cut surface.

In *size* they may vary from microscopic smallness to the dimensions of a chesnut or even larger. In the brain nearly

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[1] "Diseases of the Nervous System."—*New Sydenham Society*, 1877, Lecture VI., p. 162.

the entire area of the pons, or one of the crura, may be occupied by a sclerotic focus. The very large areas appear to be the result of a confluence of smaller original foci. The largest patch found among my cases is seen in Fig. 11.

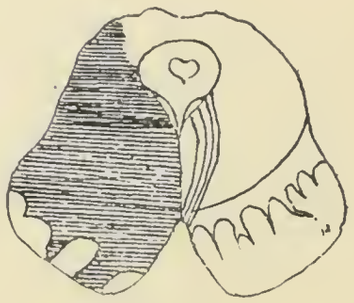

FIG. 11.

CASE XIV.—Through the middle of the superior corpora quadrigemina. The shading indicates the sclerosis. Natural size.

The *number* of nodules is very variable—a few only being observed in some cases, while in others hundreds may be counted.

The *distribution* of the diseased areas follows no known law. The patches, however, generally commence in the white substance of both brain and spinal cord. Occasionally the grey matter of the cord is selected as the primary seat. Fig. 12 shows a markedly sclerosed patch limited to the grey commissure of the cord, all the neighbouring white matter being quite healthy.

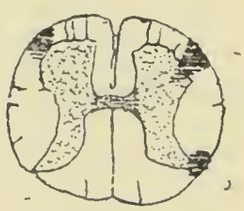

FIG. 12.

CASE VI.—Through the lumbar enlargement. From a Weigert specimen. The shading represents the sclerosis. × 2.

The grey substance of the cord, however, is not involved so frequently as the white, but it opposes no barrier to the extension of the morbid process. In Case VII., which ran a rapid course, all the sections, which I had an opportunity of examining, showed patches entirely limited to the white matter (Figs. 7, 8, 9). The sclerotic process is said never to commence in the grey matter of the cerebral cortex. In advanced cases, however,

patches occasionally invade that part, as is seen in Fig. 13. In a case reported by Taylor[1] the cortex cerebri was also involved.

The patches may be numerous and of large size in one segment of the nervous axis, and small, few in number, and even absent in others. Sometimes the patches are so numerous as to leave scarcely a single region uninvolved. This was so in cases published by Hirsch,[2] Liouville,[3] Taylor,[4] and others.

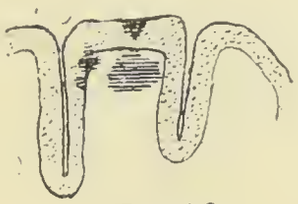

FIG. 13.

CASE XIV.—Horizontal section through the cortex in the left parietal region. The sclerosis is indicated by shading. Natural size.

The *cerebral hemispheres* often contain a large number of foci scattered in the centrum ovale, corpus callosum, internal capsule with its surrounding ganglia, and sometimes patches are situated beneath the lining membrane of the lateral ventricles. There were, however, no patches in the internal capsule, nor was there any peri-ependymal sclerosis in my cases. In Case IV., though the disease was very advanced in other regions, no sclerotic areas could be found in the cerebral hemispheres, which were divided into thin slices and carefully examined; but in my other cases patches were found in this part of the brain.

The *thalamencephalon* was involved in Case VI., patches being seen in both optic thalami. In Case I. the pituitary body seemed harder than normal. The corpora mamillaria appeared to be normal in all my cases.

The *mesencephalon* was affected in three of my cases: in Case XIV. almost one-half of the section at the level of the superior corpora quadrigemina showed sclerosis (Fig. 11); both crura contained sclerotic patches in Case IV. (Fig. 37); and the right was involved in Case VI. (Fig. 42). No patches were visible externally in any of these cases.

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[1] "Zur pathologischen Anatomie der multiplen Sklerose," Berlin, 1893.

[2] and [3] "Fox's Pathological Anatomy of the Nervous Centres," 1874, p. 119.

[4] *Loc. cit.*

The *pons varolii* was very extensively diseased in Case IV. (Fig. 36) and Case XIV. (Fig. 47), and markedly, but to a less extent, in Case I. (Fig. 32). In Case VI. the pons was only slightly implicated (Fig. 41). No marked patches appeared externally in any case, but the floor of the fourth ventricle in Case VI. presented slight alterations in colour between grey and white.

The *medulla oblongata* contained numerous foci in Case I. (Fig. 31), Case IV. (Fig. 35), and Case XIV. (Fig. 46), but here again Case VI. almost entirely escaped (Fig. 40). No distinct patches were visible externally in any case.

The *cerebellum* was not affected in any of my specimens. If patches occur here they are usually confined to the white substance.

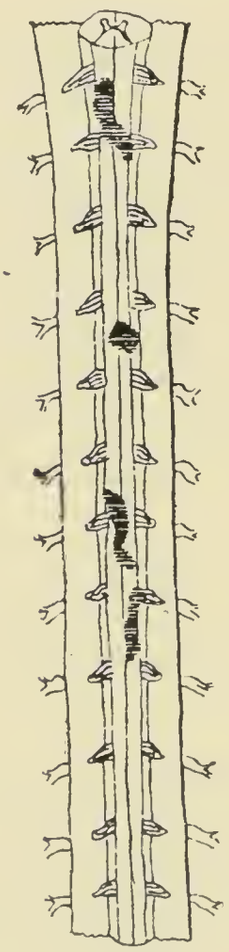

FIG. 14

CASE VI.—From a water-colour made immediately after the autopsy. Dorsal region. The sclerosis is represented by shading. Half natural size.

The *spinal cord* was considerably involved in all my cases excepting Case VII., where the grey matter entirely escaped. As regards the white matter, in some altitudes the lateral, in others the posterior, and in others the anterior columns were

chiefly implicated. The sclerosis appeared externally only in Case VI. (Fig. 14). In Case IV. every section showed sclerotic change, but in the others at certain intervals the cord was exempt from disease. The sclerosis never quite extended through the whole thickness of the cord in any of my cases; the nearest approach to a complete transverse sclerosis was seen in Case IV. (Fig. 15). Sometimes the cord appears to be

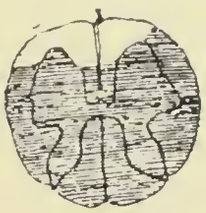

FIG. 15.

CASE IV.—Through the middle of the lumbar enlargement. The shading indicates the sclerosis. × 2.

FIG 16

CASE IV.—Transverse section through the optic nerves. The shading indicates the healthy tissue. × 4.

FIG 17

CASE IV.—Transverse section through optic chiasma. The shading indicates the healthy tissue. × 2.

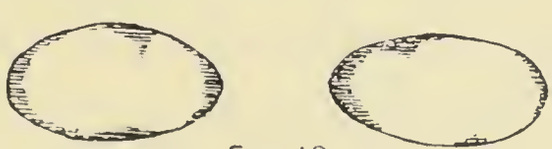

FIG 18

CASE IV.—Transverse section through optic tracts. The shading indicates the healthy tissue. × 4.

almost continuously occupied by a sclerosis of moderate intensity, and a few disseminated foci in the brain alone prove that the case belongs to this form of sclerosis.

Sclerosis of the *cranial nerves* in their course outside the brain was only seen in Case IV., and here the disease was confined to the optic nerves, optic chiasma, and optic tracts (Figs. 16, 17, 18). Other cranial nerves were examined in my

cases, but were found to be perfectly healthy. In published cases one finds that the olfactory, third, fifth, and facial nerves are those most often affected.

The *spinal nerve-roots* and the *cauda equina* were perfectly normal to the naked eye and to the touch. I had no opportunity of examining the *peripheral nerves*. Moxon[1] in one case found the brachial plexus on each side normal.

The *skull* sometimes shows sclerotic thickenings, or occasionally it is thin and eroded ; it was normal in my cases. The *membranes* are frequently normal, sometimes congested, as in Cases IV. and VI., or even chronically inflamed. According to Erb[2] the *cerebro-spinal fluid* is as a rule increased, frequently cloudy, and sometimes the *ventricles* are considerably dilated. In my cases, however, the ventricles and the ventricular fluid appeared quite normal.

The morbid appearances of the bedsores, or the complications involving the bladder, kidneys, lungs, or other organs do not differ from those seen in the later stages of other forms of chronic nervous disease.

**Microscopic Anatomy.**—For purposes of histological examination the various brains and cords were thoroughly hardened in Müller's fluid. Numerous portions of these were embedded in celloidin and sections were cut. They were systematically stained with aniline blue-black, logwood, according to Weigert's method, by Pal's method, by Pal's method together with logwood, and by a combination of Pal's method with logwood and eosin, constituting a triple stain. In a few instances carmine was employed. An examination of patches at various stages in my cases showed :—

1. In a *very early stage*, there was distinct overgrowth of the connective tissue, which was richly nucleated. The nerve fibres, enveloped by this neuroglia hyperplasia, were normal, even the myeline sheath being fairly preserved, as was especially well seen in the Weigert and in the Pal specimens.

2. In a *more advanced stage*, the connective tissue was more uniform and more closely meshed ; most of the myeline sheaths had disappeared, but a few were here and there visible, faintly stained and somewhat irregular.

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[1] *Loc. cit.*

[2] *Loc. cit.*, p. 483.

3. In a *very advanced stage*, a dense felted web of tissue, somewhat granular in appearance, was seen. There was absolutely no trace of myeline, but embedded in the small faint spaces of this tissue a few isolated axis-cylinders were not unfrequently recognised. They were, however, naked, and in direct contact with the fibrous tissue. In the most intensely sclerosed regions the axis-cylinders had disappeared, and no traces, or at best, but doubtful traces of the normal nerve tissue were left behind. That the axis-cylinders do persist, even in fairly dense sclerotic tissue, is seen in Fig. 19.

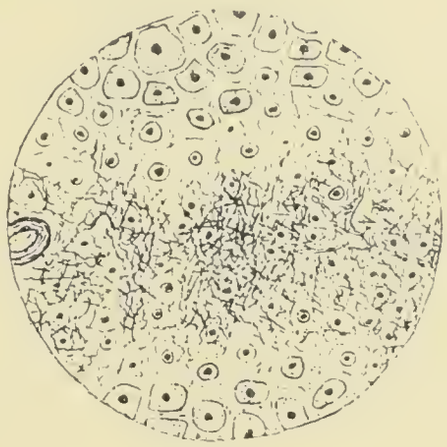

FIG. 19

CASE XIV.—From a section through a sclerotic patch stained with aniline blue black. The axis-cylinders are represented by black dots. ×325.

Many writers state that in the last phase of the sclerotic process some of the axis-cylinders become hypertrophied, increasing to twice, thrice, or even more of their diameter. Of this I could not assure myself in any of the specimens.

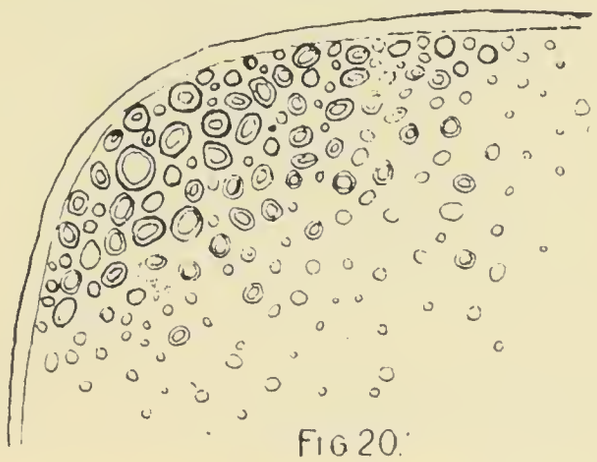

FIG 20.

CASE IV.—From a section stained by Pal's method. ×240.

Although the morbid foci appear to the naked eye to be sharply defined from the normal tissue, closer examination

showed that in many cases the areas are marked off by transitional zones, so that the diseased and healthy parts seem gradually to fuse with one another, as in Fig. 20.

Less frequently around some patches there is no transitional zone of partial disease, a patch of marked sclerosis being bounded by normal nerve tissue (Fig. 21).

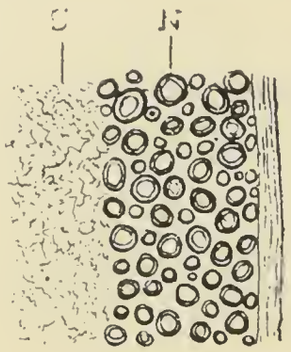


FIG 21.

CASE XIV.—From a section stained by Weigert's method. S—Sclerotic tissue. N—Normal tissue.

Degeneration of the ganglion cells in the grey matter of the cord only occurs in an advanced stage of the process. Judging from my sections these motor cells escape till long after the anterior horn is implicated. Case I. alone showed reaction of degeneration in the muscles during life. Comparing the

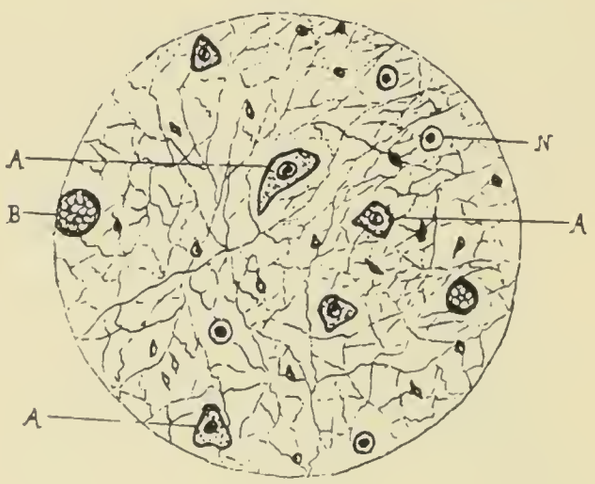


FIG 22

CASE I.—From a section stained in carmine. A—Atrophic ganglionic cells. B—Blood-vessel. N—Nerve-tubule. × 325.

anterior horns of this case with similar parts of a normal cord stained in the same way, I found changes in the ganglionic cells in the lower dorsal and lumbar regions in this case.

Pigmentation, though present in a slight degree normally, was much more marked in the diseased cells. The processes of the cells also had become rounded off, and the cells themselves considerably distorted by the pressure of the sclerotic material. In addition, the cells were much less in number than those of a normal anterior horn (Fig. 22).

In specimens from my other cases which showed no reaction of degeneration during life, the ganglionic cells differed little from the normal. This resistance of the motor cells is surprising, considering how advanced the sclerotic process was in many sections.

Numerous anterior and posterior spinal nerve-roots in three cases were subjected to histological examination. Sections were cut transversely and longitudinally, and some bits were teased. Various stains were used, but I failed to discover even the slightest trace of sclerosis in any of these roots. The cauda equina, also, in three cases, was similarly treated, but here again the examination proved negative. In very advanced cases, published by Taylor[1] and others, marked sclerosis has been found in both cauda equina and spinal nerve-roots. The olfactory lobes and the fifth nerves were microscopically examined in Case IV., but were found to be quite healthy.

Though the lesions in some of my cords were very extensive, yet there were no tracts of secondary degeneration, either ascending or descending. The preservation of the axis-cylinders even in deeply sclerosed parts is the explanation given by most writers of the absence of secondary degeneration. Such change seems possible when the axis-cylinders are completely destroyed. A very advanced patch may then cause some amount of secondary degeneration; but even here the degenerated fibres do not constitute a very compact band. Babiniski[2] has, however, related under the title of the destructive form of disseminated sclerosis, the history of a patient who presented during life all the symptoms of a circumscribed myelitis, and in whom disseminated sclerosis was found after death. The patches were remarkable for the almost complete absence of axis-cylinders, and for the presence of well-marked secondary

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[1] *Loc. cit.*

[2] *Loc. cit.*, p. 85.

degenerations. In a case described by Rovigli[1] a large transverse focus in the cord led to ascending and descending degenerations.

In two of my cases, micro-organisms were examined for, but without success. These investigations were, however, pursued not when the specimens were fresh, but after they had been hardened in Müller's fluid.

Greiff[2] has described and figured what he considered a new lesion in disseminated sclerosis, under the name of disseminated vitreous degeneration of the cerebral cortex. Other pathologists, however, are of opinion that this lesion is artificial, and consists in a precipitation of leucine crystals extracted from the brain substance by the action of alcohol.

Vascular Changes.—It is remarkable how frequently morbid changes are found in the vessels in this disease. The vessels surrounding and traversing the diseased areas are certainly often, if not always, involved. Rindfleisch[3] has stated that the centre of the grey pin-headed foci from which the sclerosis starts is always a distended blood vessel which, microscopically, is in a state of chronic inflammation. The number of blood vessels sometimes may be considerably increased. Case XIV. alone showed important vascular lesions, and this is probably due to the fact that this case ran a very rapid course, while my other cases were much more chronic in their progress.

*Changes in the Vessel Wall.*—Thickening of the walls was first pointed out by Charcot[4] in his early work. It affects usually the external adventitial coat, and in sections where the sclerosis is very pronounced the vessels are gaping and appear dilated. In other cases this sort of overgrowth of the adventitia extends inwards so as to cause fibroid degeneration of the middle coat or even of the intima, so that the whole wall appears to be sclerosed and richly nucleated. As a consequence the lumen may become narrowed, and in the smaller vessels complete obliteration has sometimes been observed, as in a case

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[1] "Rivista Sperimentale di Freniatria e di Medicina Legale," X., p. 227.

[2] *Archiv für Psychiatrie*, XIV., p. 286.

[3] *Virchow's Archiv*, 1863, Bd. XXVI., p. 474.

[4] "Diseases of the Nervous System."—*New Sydenham Society*, 1877, Lecture VI., p. 174.

published by Hess.[1] In Case I. the walls of the vessels were thicker than normal and their lumen was wide; the blood-vessels in Case IV. had also often thickened walls; and in Case XIV. the vessels in the older and firmer patches were dilated.

*Changes in the Interior of the Vessel.*—In Case XIV. there was not unfrequently seen a larger proportion of leucocytes among the red blood cells within the vessels than is normal. These leucocytes were especially numerous about the periphery of the vessel. In addition distinct thrombi were found in several of the vessels in the upper cervical region (Figs. 49, 50). Bastian[2] states that on several occasions he had found the larger vessels of a patch of spinal sclerosis blocked by an old and firm thrombus. Ribbert[3] also has twice found in a soft recent patch a partial obstruction of a vessel by a peripheral thrombus consisting of white corpuscles only.*

*Changes external to the Vessel Wall.*—In Case XIV. the perivascular lymph-sheaths in many parts were packed with round cells (Figs. 23, 24, 25).

FIG. 23.

CASE XIV.—Transverse section.

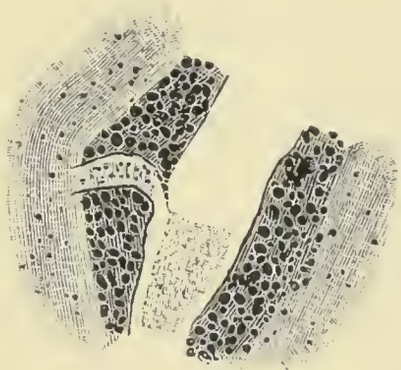

FIG. 24.

CASE XIV.—Longitudinal section.

Sections of two blood vessels, showing marked distension of the perivascular lymph sheaths with round cells. (From drawings by Dr. Williamson.)

A similar distension of these lymph spaces has been reported in many other cases, and it is possible that this extravasation

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[1] *Archiv für Psychiatrie*, Berlin, 1887, XIX., p. 64.

[2] "Quain's Dictionary of Medicine," Vol. II., p. 845.

[3] *Virchow's Archiv*, Bd. XC., p. 243.

* I have just discovered a thrombus — similar to that figure on page 124 — in one of the anterior median veins in the dorsal region of the cord in Case IV (see specimens).

of leucocytes may be one of the initial steps in the development of the disease. In Case XIV. also, in the soft recent patches, dilated vessels, with distended lymph-sheaths, were surrounded by an enormous number of round cells (Fig. 25).

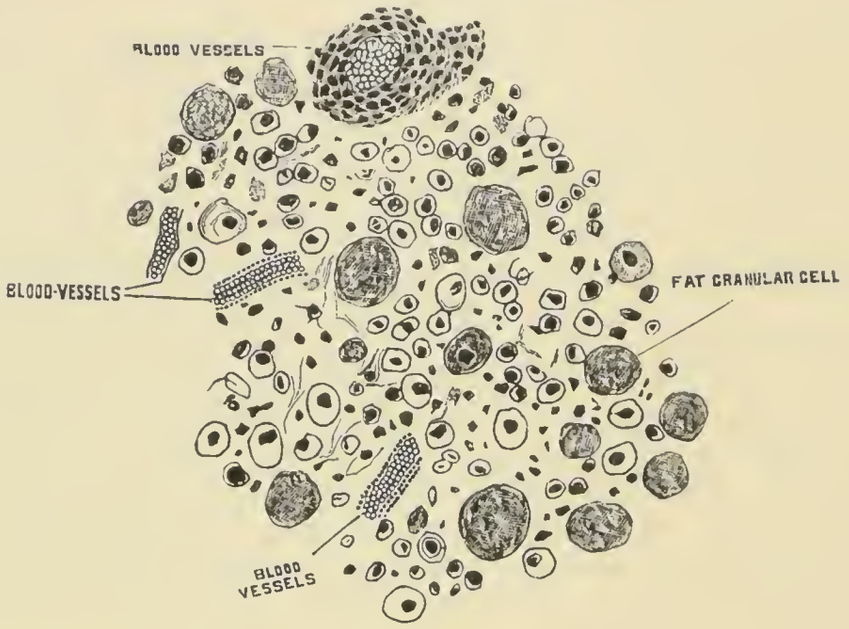


Fig. 25.

Case XIV.—Section through the centre of a softened patch in the white matter of the cerebrum just beneath the cortex. The section shows dilated blood vessels and cell elements. Nerve fibres are absent, and only few neuroglia fibres are seen. (From a drawing by Dr. Williamson).

In somewhat older patches in the same case, the tissue immediately outside the perivascular lymph-sheaths sometimes appeared to be infiltrated with round cells (Fig. 26).

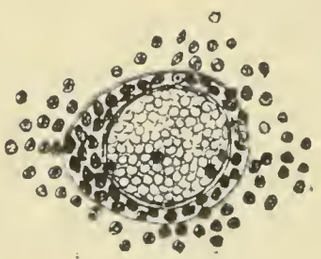

Fig. 26.

Case XIV.—From a section through the lower cervical region of the cord, stained by logwood. Showing round cells external to the perivascular lymph-sheath. ×325.

*Hæmorrhages* in the brain or cord have been occasionally observed. In Case VI. a well-marked hæmorrhage was found in the right centrum ovale minus, and was due to rupture of a small vessel (Fig 27).

Marked vascular changes have also been observed by Buss,[1] Déjérine,[2] Demange,[3] Köppen,[4] and others.

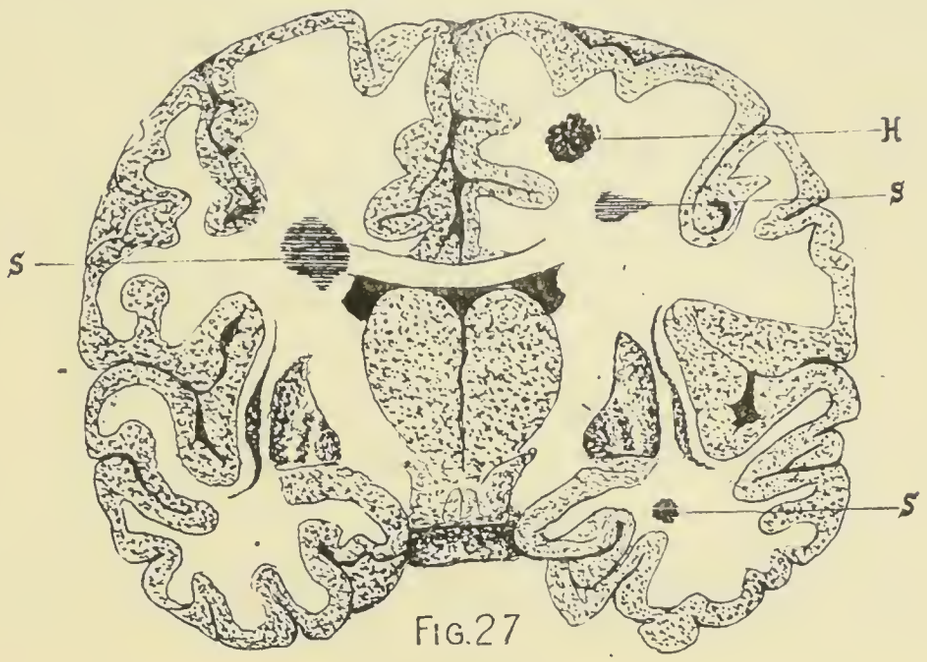


FIG. 27

CASE VI.—Vertical section of the brain at a level with the posterior part of the internal capsule. H = Hæmorrhage. S = Sclerotic patch. × ½.

## MORBID ANATOMY OF CASE I.

*Abstract of Autopsy* (April 28, 1891).—The body was exceedingly emaciated. Bedsores were seen over the sacrum, hips, internal surfaces of the knees, left heel, and tips of toes. Pleuræ normal. Healed phthisis at the apex of the right lung. The left lung presented purulent foci at its apex and enlarged caseating glands at the left hilus, and the lower lobe was partly consolidated by disseminated patches of caseous pneumonia. The kidneys were deeply congested, and the bladder walls were in a condition of acute cystitis. The membranes of the brain were normal, and the cerebral cortex showed no trace of disease. The pituitary body was somewhat enlarged, and firmer than usual. The meninges were more adherent to the spinal cord than normal. No sclerotic patches visible externally. The brain and cord were placed in Müller's fluid.

*Cord.*—On section scattered areas of sclerosis were found in all regions. In the upper half of the cord, however, the grey matter seemed entirely free from sclerotic change, but in the

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[1] *Deutsches Archiv f. klin. Med.*, Bd. XLV., p. 555.

[2] *Revue de Méd.*, 1884, p. 193,

[3] *Ibid.*, 1884, p. 193.

[4] *Archiv für Psychiatrie*, Bd. XXVII., p. 63.

lower dorsal and lumbar portions the grey matter, especially that of the anterior horns, was implicated to a considerable degree. In the cervical region the chief patches of sclerosis were seen in both posterior columns and in the left lateral column (Fig. 28). In the dorsal region the posterior columns

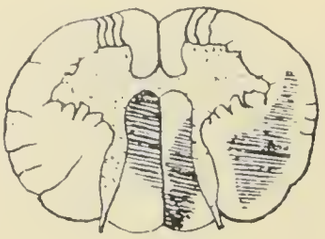

Fig 28

Case I.—Through the cervical enlargement. The shading indicates the sclerotic patches. × 2.

were again involved, and there was a well-marked patch in the right pyramidal tract (Fig. 29). Lower down in the dorsal

Fig 29.

Case I.—Through the mid-dorsal region. The sclerosis is represented by shading. × 2.

region the anterior horns of grey matter were diseased. In the lumbar region, the posterior, and both lateral columns of white

Fig 30.

Case I.—Through the lumbar enlargement. The shading indicates the sclerosis. × 2.

matter, and both anterior horns of grey matter, showed sclerotic change (Fig. 30). There was no ascending or descending degeneration.

The *medulla* contained many sclerotic patches, somewhat less numerous towards the upper part (Fig. 31).

The *pons* showed many small foci of disease. At about the middle of the fourth ventricle some four or five patches of sclerosis could be seen (Fig. 32).

No patches were present in the mesencephalon or thalamencephalon.

*Cerebral Hemispheres.*—The upper surface of the left lenticular nucleus presented a sclerotic patch not involving the internal or external capsules. No patches could be found in the corona radiata. Cranial nerves, anterior and posterior roots, and cauda equina normal.

FIG 31

CASE I.—Through the middle of the olivary body. The shading is in the situation of the sclerotic areas. × 2.

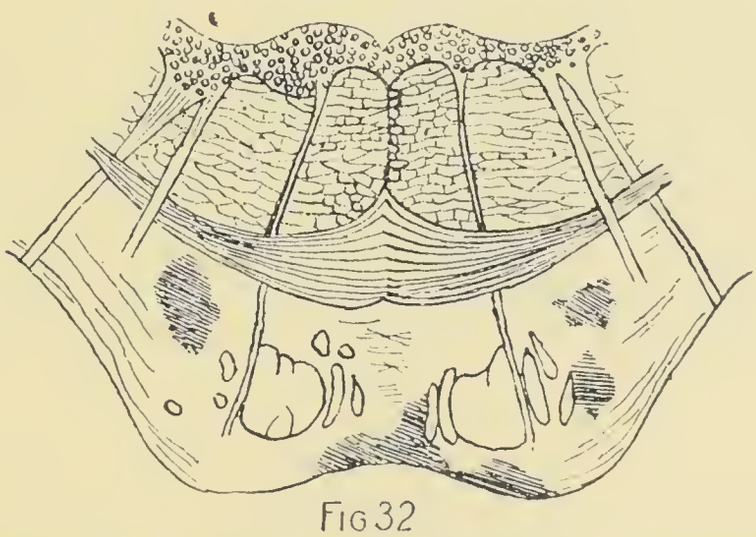

FIG 32

CASE I.—Through the middle of the fourth ventricle. The sclerotic patches are shaded. × 2.

The *histological* appearances of the disease agreed in most points with the general description previously given. Sections through the lumbar and lower dorsal regions of the cord showed atrophic change in the anterior motor ganglionic cells (Fig. 22). The vessels showed very little change. Those running through a sclerotic patch were somewhat distended, and their walls appeared to be thicker than normal. Micro-organisms were not examined for, neither was Popoff's stain employed.

## Morbid Anatomy of Case IV.

*Abstract of Autopsy* (December 28, 1893). Partial examination only was allowed, no permission being obtained to open the chest or abdomen. The body was extremely wasted throughout. There were extensive bedsores over the sacrum, tuberosities of ischia, left great trochanter of femur, over the internal condyle of each femur, and on both heels, exposing the posterior surface of the os calcis. The legs were flexed by muscular contractures at the hip- and knee-joints. The membranes of the cord were slightly congested. The cord itself was well developed, but somewhat firmer than usual. The cerebral dura mater was slightly adherent to the skullcap, but not markedly hyperæmic. The pia and arachnoid coverings were somewhat opaque, slightly thickened, a little congested and œdematous. The cortex cerebri was well developed and appeared normal. There were no external evidences of disease on the crura, pons, medulla, or cord. On making a number of transverse cuts across the cord, numerous areas, irregular in size, shape, and distribution, of a yellowish-grey colour and somewhat gelatinous looking, were seen throughout, but especially in the lumbar region. The brain and cord were placed in Müller's fluid.

*Cord.*—The cervical region showed extensive disease. In higher sections the only healthy portions of the white matter were the anterior columns, the anterior part of the left pyramidal tract, and a small area in the right postero-internal column just below the commissure. The left posterior horn of grey matter was markedly sclerosed, and the right posterior horn and the grey commissure were also involved, but to a less extent. About the middle of the cervical enlargement the distribution of the sclerosis was as indicated in Fig. 33.

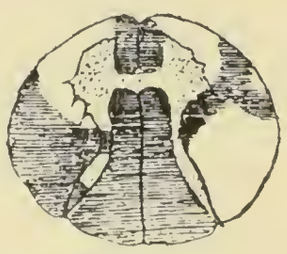

Fig. 33.

Case IV.—Through the cervical enlargement. The shading represents the sclerosis. × 2.

The lower cervical sections showed the grey matter and both posterior columns to be fairly normal. The anterior columns and the right crossed pyramidal tract, however, were extensively diseased. In the upper dorsal region the sclerosis again

became more pronounced posteriorly, and the anterior columns and horns were very little involved. Mid-dorsally the extent of the sclerosis was as depicted in Fig. 34.

FIG. 34

CASE IV.—Through the mid-dorsal region. The shading indicates the sclerosis. × 2.

In the lower dorsal region the right antero-lateral columns were fairly healthy, and there was a circumferential ring of healthy tissue in the posterior half of the section. The remainder showed marked sclerosis. Coming to the lumbar portion of the cord one found very extensive sclerotic change, in some of the upper sections there was scarcely any healthy tissue remaining. Lower down the whole transverse section was almost one interrupted mass of sclerosis (Fig. 15). There was no ascending or descending degeneration.

Every section through the *medulla* displayed sclerotic areas. In the upper part six large patches were seen (Fig. 35).

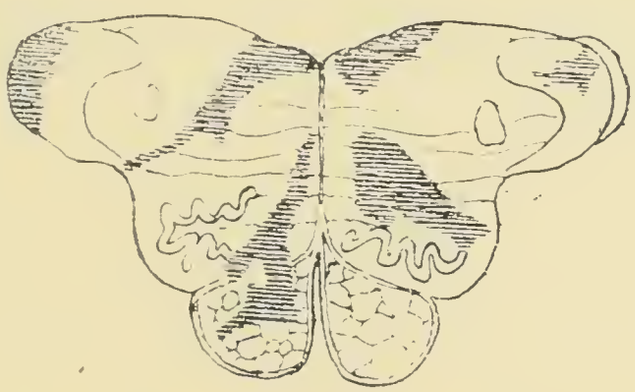

FIG 35

CASE V.—Through the upper portion of the medulla. The shading represents the sclerosis. × 2.

The *pons* also showed numerous patches at every level. In its lower regions the sclerotic changes were very extensive (Fig. 36).

Both *crura* were involved to the extent shown in Fig. 37.

The rest of the brain was cut vertically into thin slices and very carefully examined. No sclerotic patches, however, could be found.

On *histological examination* of the sclerotic patches, the more minute structures were found to coincide with the general

description already given. One curious feature was that, although the grey matter of the cord was so extensively diseased, the large motor ganglion cells showed little or no change, and the number of these cells seemed also about normal. Many of the vessel walls in the neighbourhood of the patches appeared to be thicker than usual; but no embolism, thrombosis, or even distension of the perivascular lymphatic spaces were to be seen. The chronicity of the case probably accounted for the lack of vascular changes. Many anterior and posterior spinal

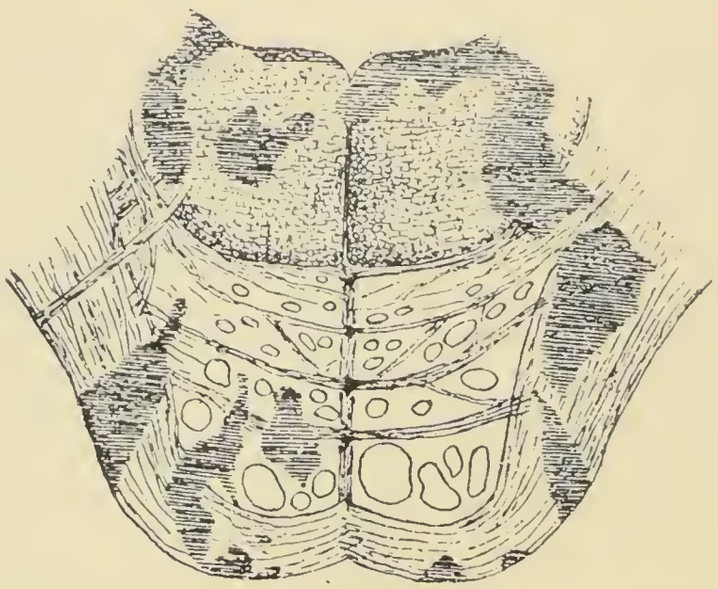

FIG. 36.

CASE IV.—Through the lower half of the pons. The sclerosis is indicated by shading. × 2.

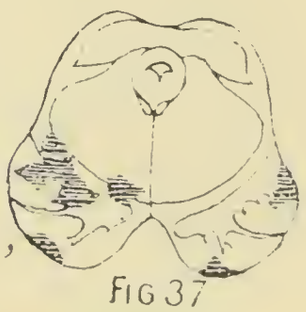

FIG 37

CASE IV.—Through the inferior corpora quadrigemina. The shading marks the sclerotic areas. Natural size.

nerve-roots were microscopically investigated, but no sign of disease could be made out. An examination also of transverse and longitudinal sections through the cauda equina was negative. There was very marked sclerosis of the optic nerves, optic chiasma, and optic tracts (Figs. 16, 17, and 18). Both olfactory lobes and the fifth nerves were microscoped and found normal. Some sections through sclerotic patches were stained by Popoff's method, and some of these were teased, with the result already mentioned. A search for micro-organisms proved unsuccessful.

* See foot-note on page 109.

## Morbid Anatomy of Case VI.

*Abstract of Autopsy* (June 8, 1894).—Body well nourished. Slight lateral curvature of the spine, with exaggeration of the antero-posterior curve. The pleura was slightly adherent at the left apex, the lungs were congested, and there was a small tubercular focus at the left apex. Bronchi congested. Extensive septic cystitis and distinct septic pyelo-nephritis. The meninges of both brain and cord were considerably congested. On the cord, externally, were seen four areas of a darker

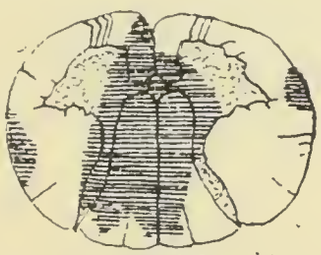

Fig. 38.

Case VI.—A little below the middle of the cervical enlargement. The shading represents the sclerosis. × 2.

colour (Fig. 14). These were irregular in size, shape, and extent. and were limited to the anterior surface of the dorsal region. The floor of the fourth ventricle presented slight alterations in colour, between grey and white. The brain and cord were placed in Müller's fluid.

*Cord.*—High up in the cervical region a patch was seen in the right anterior column, and a little lower down a sclerotic area was observed surrounding the left posterior horn. The cord

Fig. 39.

Case VI.—Through the mid-dorsal region. The sclerotic patches are indicated by shading. × 2.

was free from sclerotic change for some little distance, and then the posterior columns were densely sclerosed, and at the same level the left lateral column was slightly diseased. About the middle of the cervical enlargement, three more patches were met with (Fig. 38). There was then a long interval before another patch was visible, and this was situated in the posterior columns, low down in the cervical region. There were three patches in the upper dorsal, one in the posterior columns and one around each anterior horn. Mid-dorsally, the disease was as represented in Fig. 39. A little further down, only the right

posterior column was affected, and about half an inch lower the sclerosis was confined to the anterior columns. Just inferior to this, a patch was found in the left lateral column. In the lowest dorsal region, sclerosis was seen in the right posterior column. The lumbar portion of the cord was very free from disease. In the upper portion there was only

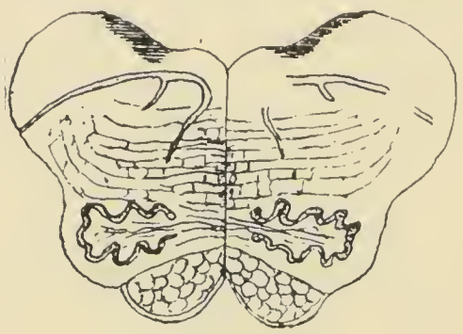

FIG. 40.

CASE VI.—Through the lower portion of the medulla. The shading represents the sclerosis. × 2.

slight sclerotic change in the posterior columns, and a little lower the disease was limited to a small focus in the grey commissure, a patch in each lateral column, and another patch slightly implicating the posterior horn with the adjoining white matter (Fig. 12). There was no ascending or descending degeneration.

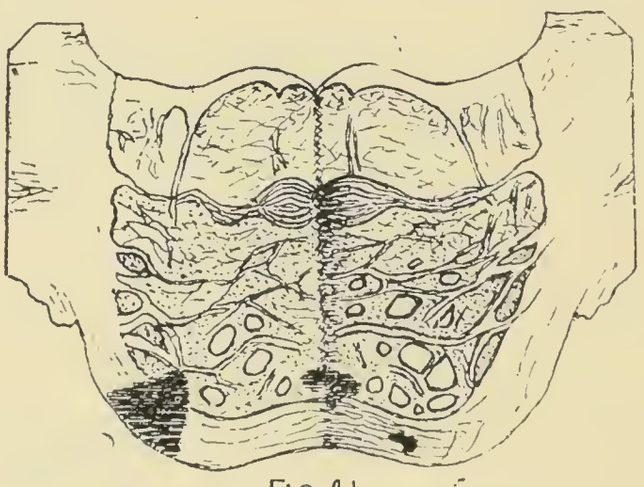

FIG. 41.

CASE VI.—Through the middle of the fourth ventricle. The sclerosis is indicated by shading. × 2.

In the *medulla* a few small sclerotic areas only are to be seen (Fig. 40).

In the *pons* the disease was also very slight (Fig. 41).

*Mesencephalon.*—The right crus presented distinct sclerotic patches (Fig. 42).

*Thalamencephalon.*—Several sclerotic foci were seen in both optic thalami.

*Cerebral Hemispheres.*—Seven patches were found in the centrum ovale. Three of these were seen in a vertical section of the brain, at a level with the posterior part of the internal capsule (Fig. 28). In this section a small hæmorrhage was also observed in the upper portion of the left centrum ovale minus. Another sclerotic patch, in a section a little anterior to the previous one, was situated about the middle of the left lenticular nucleus.

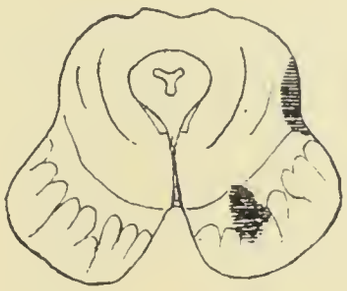

FIG. 42.

CASE VI.—Through the middle of the superior corpora quadrigemina. The shading represents the sclerosis. Natural size.

The *histological appearances* of the patches agreed with the general description already given. The vessels showed little or no change excepting for the small hæmorrhage already mentioned (Fig. 28). Microscopical examination of this showed rupture of a small vessel with extravasated blood all around. The anterior and posterior spinal nerve-roots, cauda equina, and the cranial nerves appeared healthy. No micro-organisms were found. Popoff's stain was employed here also (Fig. 10).

CASE XIV.*—Joseph T., aged 23, was admitted as an in-patient at the Manchester Royal Infirmary, under the care of Dr. Ross, February 24, 1891.

*Previous History.*—In the early part of 1890 the patient occasionally felt sensations of numbness in the left hand and breast, especially when cold ; but in the summer these sensations disappeared. He also noticed that his sight was not so good as previously. In November, 1890, he got his feet very wet whilst working in a damp place. His clothes also got very wet, and he continued his work without changing them. Soon afterwards he noticed a sensation of numbness in his left big toe, which spread upwards. A few days later he began to feel ill and stiff, and was unable to continue work. He was seen by a medical man on December 27, 1890, who found that he was suffering from acute rheumatism. The

* From the *Medical Chronicle*, March, 1894. I am indebted to Dr. Williamson for some of the notes, several of the drawings, and generous permission to work at the brain and cord of this case.

attack was a very severe one, but he improved rapidly under salicylate of sodium. It was not until he had recovered from the attack of rheumatism that distinct symptoms of sclerosis appeared. He was able to walk about his room quite well after recovering from the rheumatism; but at the end of January, 1891, he noticed a well-marked sensation of numbness in the left side. He also noticed loss of power in his left leg and arm, and his sight began to fail, so that reading became difficult. The left arm and leg gradually became more paralysed, and about two weeks after the onset of paralysis on the left side, the right leg became paralysed. Afterwards (*i.e.*, shortly before he came to the Infirmary) he "lost the power of grasping objects with his right hand." There was no history of alcoholism or syphilis.

*State on Admission* (Feb. 24, 1891).—Patient is a well-nourished, healthy-looking man. Mentally, he is dull and confused. His answers are somewhat contradictory. He is restless and irritable. His speech is "scanning." The right palpebral fissure is smaller than the left, and the right pupil is also less than the left. Both pupils react to light and accommodation. There is nystagmus on looking to the right. Rotation of eyeballs to the right is good, but on attempting to look to the left there is only slight external rotation of the left eye and no rotation of the right eye (to the left). On looking upwards the right eye is not raised so high as the left. Ophthalmoscopic examination: fundi normal. The grasp and all the movements of the left arm are feeble. The movements of the right arm are fairly good. Movements of left leg feeble; complete paralysis of the right leg. Rigidity of the left arm, and slight rigidity of both legs to passive movements. Knee-jerks both increased; ankle-clonus on both sides. Plantar reflexes both present. Abdominal, epigastric, and cremasteric reflexes absent. There are frequent attacks of marked tremors in both legs. The tremor affects the whole of the limbs, and is arrested by flexing the big toes. There is marked unsteadiness and tremor of both arms when the patient performs any voluntary movement, such as touching the tip of the nose with the index finger. There is retention of urine, which has to be drawn off by a catheter twice daily. There is incontinence of fæces. Urine, 1012, alkaline; a trace of albumen present; no sugar. There is a deposit of phosphates, but no pus could be detected. Nothing noteworthy with respect to the condition of the heart and lungs.

On admission, the temperature was normal (Feb. 24), but from the evening of Feb. 25 it gradually rose.

| | | Temperature. | | Temperature. |
|---|---|---|---|---|
| February 26. | Morning ..... | 100·0° | Evening..... | 100·2 |
| „ 27. | „ ..... | 100·4° | „ ..... | 101·6 |
| „ 28. | „ ..... | 101·4° | „ ..... | 102·6 |
| March 1. | „ ..... | 101·2° | „ ..... | 104·0 |

On the 28th the pulse was 144; respiration, 26. The patient became rather dull and drowsy, but his other symptoms remained just the same. Death occurred on March 1.

*Abstract of Autopsy.*—Skullcap, dura mater, and base of skull normal. Externally, the brain appears normal. On section in the right frontal lobe—in the white matter just beneath the cortex of the middle frontal convolution—is a roundish greyish-yellow patch, about the size of a marble. It is very soft and gelatinous. In the white matter, at the centre of the left

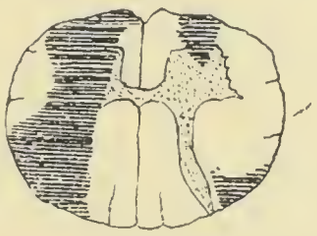

FIG. 43

CASE XIV.—Through the middle of the cervical enlargement. The shading indicates the sclerosis. × 2.

occipital lobe, is a similar patch, about half an inch in diameter. In the right temporo-sphenoidal lobe, situated in the white matter just beneath the middle convolution, is a very soft, almost diffluent, patch, of a greyish-yellow colour, and about one inch in diameter. From the cut surface, a small quantity of turbid greyish fluid escaped. There is a similar patch beneath the upper part of the right ascending frontal convolution. These two patches closely resemble ordinary cerebral softening.

FIG. 44.

CASE XIV.—Through the middle of the dorsal region. The sclerosis is represented by shading. × 2.

The cerebellum contains no sclerotic patches. External appearance of the spinal cord, normal. In the thoracic and abdominal organs there are no changes of importance. The brain and cord were placed in Müller's fluid.

*Cord.*—In the highest cervical region, there were three patches of sclerosis, one in the left and two in the right lateral column. A little lower a sclerotic area was seen, involving the anterior horn and surrounding white matter. About the middle of the cervical enlargement, there were three patches of sclerosis (Fig. 43). In the lower cervical region, the sclerosis was seen

to extend over about two-thirds of the transverse section of the cord. The middle half of the dorsal region showed extensive sclerosis (Fig. 44), but the remainder of this region seemed exempt from disease. In the higher lumbar

FIG. 45.

CASE XIV.—Through the upper lumbar region. The sclerosis is indicated by shading. × 2.

regions, the sclerosis was chiefly situated in the lateral and posterior columns (Fig. 45). Scattered irregularly through the *medulla*, were numerous patches of sclerosis (Fig. 46).

FIG. 46.

CASE XIV.—Through the lower portion of the medulla. The shading represents the sclerosis. × 2.

The *pons* contained a considerable number of patches. A section through its upper portion showed a very large patch on the left side, and some six smaller ones in addition (Fig. 47).

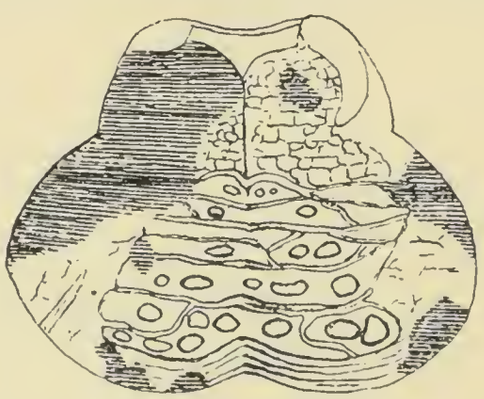

FIG. 47.

CASE XIV.—Through the upper portion of the pons. The shading indicates the sclerosis. A little larger than normal.

There was also a very large patch in the left crus (Fig. 11).

*Histological Examination.*—The firm patches in the cord presented the usual appearances of disseminated sclerosis. The

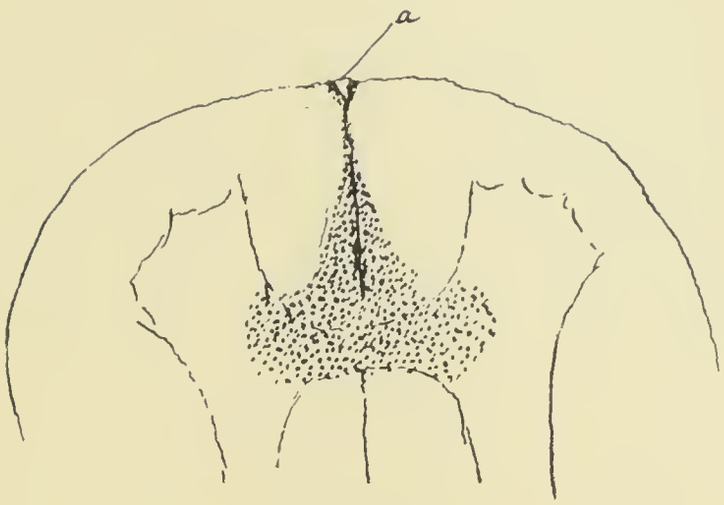


FIG. 48.

CASE XIV.—Recent patch in the upper cervical region of the spinal cord in the area of distribution of the anterior median vessels. $a$ = Thrombosed anterior median. Low power. Logwood stain. (From a drawing by Dr. Williamson.)

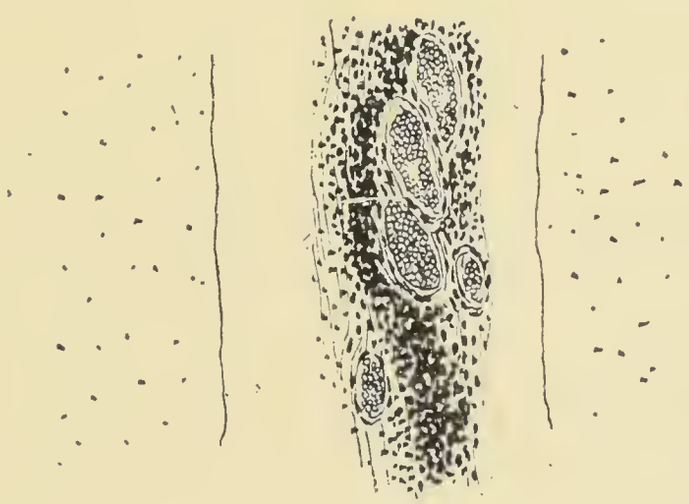

FIG. 49.

CASE XIV.—Blood vessels at the bottom of the anterior median fissure in the section represented in Fig. 48. The vessels are dilated and surrounded by numerous nuclei and round cells. High power. Logwood stain. (From a drawing by Dr. Williamson.)

blood vessels traversing them, however, were dilated, and in some parts the perivascular lymph sheaths contained round cells (Figs. 23 and 24). There was no secondary degeneration. The most recent patch in the cord was found in the neighbourhood of the anterior fissure in the upper cervical region (Fig. 48). This patch was seen to be densely infiltrated with round cells and nuclei, and was apparently being supplied by the anterior median vessels. The latter were dilated and surrounded by numerous nuclei and round cells (Fig. 49). At the upper limit of the cervical region a distinct thrombus, consisting largely of leucocytes, was discovered in the anterior median

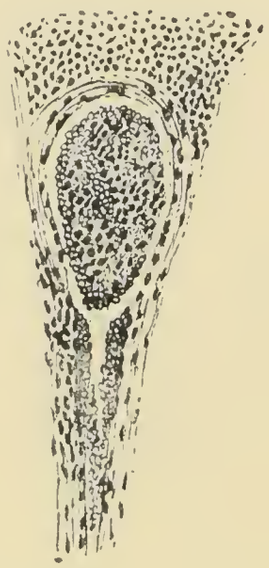

Fig. 50.

Case XIV.—Thrombosed vessel at the commencement of anterior median fissure. High power. Logwood stain. This is the vessel marked *a* in Fig. 48. The black dots = nuclei of leucocytes. The small circular = red corpuscles. (From a drawing by Dr. Williamson.)

vein (Figs. 48 and 50). At this level also several thrombosed veins were seen in the pia mater.

Sections of the soft patches in the white matter of the cerebral hemispheres presented quite a different appearance (Fig. 25). Staining according to Weigert's method showed the absence of nerve fibres at these parts. The diseased patches were seen to consist almost entirely of round cells, both at the centre and at the periphery; and there was no new formation or increase of the neuroglia connective tissue. Examination with a high power revealed the following variety of cells:—(*a*) Compound fat granular cells, many of which were of great size; (*b*) large round or oval cells, with granular protoplasm and one nucleus—many contained fat granules; (*c*) smaller round cells—leucocytes; (*d*) a few nuclei surrounded

by a small amount of protoplasm (neuroglia cells); (*e*) at some parts red blood corpuscles were mingled with the cell elements. The first three varieties were most numerous. Scattered fine fibres of neuroglia connective tissue were also seen. The blood vessels were numerous and greatly dilated. Their walls were thickened with nuclei and the perivascular sheath enormously distended with round cells. The capillaries were greatly distended and the nuclei of their walls increased.

In some of the cerebral patches, the changes were intermediate between those just described and those of the older patches in the spinal cord. They presented a slight increase of neuroglia at the centre, whilst at the outer part of the patches, cell elements were very numerous, and here again many large compound granular cells were visible.

The cranial nerves, anterior and posterior spinal nerve-roots, and the cauda equina appeared quite normal. No micro-organisms were found.

### PATHOGENESIS OF DISSEMINATED SCLEROSIS.

As regards the primary step in the formation of these patches of sclerosis, there exists much difference of opinion among pathologists. That the process is interstitial in origin is the view entertained by the large majority, but by some it is still considered to commence in the parenchymatous portions of the central nervous system. Ziegler[1] says that there is no doubt that in many cases the disease begins as a degeneration, depending primarily on a disturbance of nutrition, and first affecting the cell-elements.

To those who favour the interstitial origin, the question arises —What starts this overgrowth of connective tissues? The view expressed by Rindfleisch,[2] and more recently advocated by Ribbert,[3] and by Marie,[4] that disseminated sclerosis is a sclerosis of vascular origin appears to be exceedingly probable. The remarkable irregularity in the distribution of the sclerotic areas, showing no relation whatever to the course of nerve tracts, or to other structural arrangement of nerve tissue, seems only explicable by the vascular theory. It has been noted by

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[1] "Text-book of Pathological Anatomy." English Edition, 1886, Chap. XCIV. Art. 650.

[2] *Loc. cit.*, p. 474.

[3] *Loc. cit.*, p. 243.

[4] "Les Maladies de la Moelle." Paris, 1892, p. 160.

Rindfleisch,[1] and many others, that a blood vessel frequently occupies the centre of a sclerotic patch, the increase in the size of the patch takes place in a concentric fashion around this vessel, and the nerve tissue bounding the sclerotic patch is apparently quite healthy. The fact that new sclerotic foci may arise even in the last stages of the disease is another point in favour of this view, and finally, as seen in Chapter I., disseminated sclerosis is not unfrequently consecutive to an acute febrile affection. Ribbert[2] and Marie[3] both suggest that the process may be of an embolic nature, but up to the present time no true emboli have been found, nor has a condition likely to give rise to embolism been shown to have any relation to disseminated sclerosis.

Disseminated sclerosis has been stated to develop as a sequel of an acute myelitis, or encephalitis, by Leyden,[4] Ziegler,[5] Singer,[6] and others. In a case reported by Singer a unilateral optic nerve atrophy of central origin occurred after recovery from an acute inflammation of the cord, which proved that sclerotic foci may develop secondary to an acute process.

Westphal[7] believed that obstruction to circulation, both of blood and lymph, in the cord may act as a predisposing factor in the production of disseminated sclerosis. He rests his opinion on a case where the cord had been compressed by a tumour, and sclerotic foci of probably later date were found in the neighbouring segments of the cord.

As previously stated, disseminated sclerosis not unfrequently follows an acute febrile attack. During the fever, micro-organisms, or, what is more likely, products developed from them, are passed into the circulation. These products are of an irritant toxic nature, probably allied to albumoses and peptones, and they attack the endothelial cells of the smaller vessels. Heidenhain[8] has come to the conclusion that bodies of this nature exert

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[1] *Loc. cit.*

[2] *Loc. cit.*

[3] "Les Maladies de la Moelle." Paris, 1892, p. 160.

[4] *Zeitschrift f. klin. Med.*, Bd. XXI., H. 1 and 2.

[5] "Lehrbuch der Speciellen pathologischen Anatomie." Jena, 1887.

[6] *Präger med. Woch.*, 1885, No. 8.

[7] *Archiv für Psychiatric*, III., p. 376, IV.

[8] See Woodhead's paper, p. 629.

such a stimulating effect on the capillary walls, and also, probably, on the endothelial cells of larger vessels, that a true secretory process is accelerated, and a larger quantity of lymph than normal is thrown out. Sims Woodhead[1] has also recently shown that injection of albumoses and peptones into the blood gives rise to an outflow of lymph. The cerebro-spinal capillaries and smaller vessels have walls of extreme delicacy and activity, and a stimulation or irritation of their endothelial cells would give rise to a greatly increased outward flow of lymph. It has for long been known that whenever there is a greatly increased flow of lymph from vessels, there is also a wandering out of leucocytes. These accumulate near the vessel walls, so that at this stage the perivascular lymph sheaths are seen tightly packed with leucocytes (Figs. 23, 24). These very delicate sheaths are readily permeable, and the round cells are driven through them by the outward flow of lymph. This stage is seen in Fig. 26, which shows the lymph-sheaths distended with leucocytes, and outside this again a round-cell infiltration arranged somewhat concentrically. The exudation from the vessels either induces a swelling of the myeline, which ruptures the delicate investing albuminous sheath, or possibly acts directly on the sheath by pressure. This disintegrated myeline may partly be dissolved in the exudation, but for the most part is taken up by the white blood corpuscles, which thus become myeline carriers, and fat granular cells (Fig. 25). The neuroglia next is broken up into a granular detritus, and removed by the white blood corpuscles. The axis-cylinders are the last to go, and unless the cell infiltration is very pronounced they escape entirely. They had, however, disappeared in the centre of the soft patches mentioned in Case XIV. (Fig. 25). After a time a considerable number of round cells take on the character of fibro-blasts, and by their proliferation and growth new fibrous tissue is gradually elaborated. The morbid agent appears to persist in the patches, and to be capable of spreading to other parts. This is evident by the fact that compound granular cells (Fig. 25) are to be often seen at the periphery of the older sclerotic patches, and in the centre in the more recent foci. In those cases where thrombosis has been noticed, an increased outflow of lymph, with

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[1] *Brit. Med. Jour.*, Sept. 22, 1894, p. 630.

migration of round cells, may result from the obstruction to the vein (Fig. 50). The arterial obliteration occasionally seen might, as Hess[1] suggests, lead to the occurrence of nutritional changes, proliferation of the neuroglia, and disappearance of the myeline of the nerve fibres.

There are several facts which apparently oppose this view. Thus the percentage of cases of acute febrile disease which are followed by disseminated sclerosis is, comparatively speaking, small. It may be that, in many of these fevers, the toxic bodies are not formed in sufficient intensity to irritate the lining of the vessel walls, and start the round cell infiltraton. In other cases, where the nervous disease has come on immediately after an injury, it may possibly be that the initial stages of the process had been started by some febrile disease contracted earlier in life; the lesions not being severe enough to cause marked symptoms, the disease remained dormant until the injury re-started it into activity. Other cases of disseminated sclerosis give a history of syphilis. If, however, syphilis ever causes the disease an endarteritis may be the primary step.

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[1] *Loc. cit.*

# CHAPTER VI.

## COURSE, DURATION, TERMINATION, PROGNOSIS AND TREATMENT OF DISSEMINATED SCLEROSIS.

### COURSE OF DISSEMINATED SCLEROSIS.

CHARCOT[1] divides the clinical history of cases of disseminated sclerosis into three periods The first extends from the initial symptoms down to the supervention of rigidity of the limbs; the second stage is that of the completely developed disease; while the third commences with the failure of the nutritive functions.

In my 33 cases there is no mention in the notes of any remission or period of apparent arrest occurring after the disease had become well established. In the earlier history of many of these cases, however, an initial symptom like paresis of a limb would often clear away spontaneously, and a long interval would frequently intervene before this symptom recurred, or others took its place. Case VI. especially, affords a very good example of this. The patient's left hand became feeble and remained so for a month. It then completely recovered its power and nothing was noticed until four years later, when paresis attacked the left leg. In published cases, one not unfrequently finds that the morbid progress, under favourable influences and possibly treatment, may be temporarily arrested. In these periods of remission the symptoms may remain quiescent for many months, and even for years. Bourneville and Guérard[2] publish four cases in which the remissions were so complete as to enable the patients who had been paralysed to resume their occupation. Remissions are, however, not very common in children suffering from disseminated sclerosis, and

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[1] "Diseases of the Nervous System," *New Sydenham Society*, 1877, p. 209.

[2] *Loc. cit.*

this is not to be wondered at when one considers that the child's nervous system is in an unstable and highly vascular condition of development and growth. They were noticed in cases by Dickenson,[1] Schüle,[2] and Wilson.[3]

### DURATION OF DISSEMINATED SCLEROSIS.

The duration of the disease is very variable. In six of my cases it ranged from twelve months to ten years. Case I. lived seven years after the appearance of the first symptoms, Case IV. five years, Case V. fifteen months, Case VI. ten years, Case VII. fourteen months. Case XIV. ran the most rapid course of all, namely, twelve months. A temporary numbness of one side was first noticed twelve months before death, and slight and indefinite symptoms five months before death; but it was only after the attack of acute rheumatism (two months previous to death) that the symptoms became well defined. The most rapid case that Gowers[4] has known was fatal a year and three-quarters from the onset. If the cord only be affected life may be prolonged for twenty years or more, as in a case published by Morris[5] in which the patient lived twenty-four years after the commencement of the disease. Bourneville[6] relates three cases of disseminated sclerosis where the disease lasted fourteen, twenty-one, and twenty-eight years.

### TERMINATION OF DISSEMINATED SCLEROSIS.

Death from disseminated sclerosis *per se* is not a common occurrence, but the general impairment of nutrition resulting from the bedridden state, or the supervention of bladder troubles, or of bulbar paralysis with consequent inability to take food, or of pulmonary or other complications, may in any case give rise to a fatal termination. Occasionally death has taken place suddenly — apparently from cardiac failure. In

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[1] *Loc. cit.*

[2] *Loc. cit.*

[3] *Brit. Med. Jour.*, 1876, II., p. 675.

[4] "Diseases of the Nervous System," 1886, Vol. II. p. 514.

[5] *Loc. cit.*

[6] "Nouvelle Étude sur Quelques Points de la Sclérose en Plaques Disséminées," 1869.

some of these cases extensive disease has been found in the medulla, especially in the situation of the vagal nucleus. In children, convulsions may abruptly precipitate a fatal result.

The termination of the disease in Case VI. was interesting. This patient gradually became comatose. The temperature rose to 101·5°, the pulse quickened to 176, the face was flushed and perspiring, the conjunctivæ injected, there was conjugate deviation of the eyes to the right, the pupils were equal and reacted to light, and the corneal reflex was present. There were no true convulsions, but occasional twitchings of the limbs, with frequent spasmodic retraction of the head took place. The knee-jerks and ankle-clonus were present on both sides. When the arms were lifted up they dropped down at once, but there was no evidence of weakness on one side, or of facial paralysis. The respirations, which were regular and 40 to the minute early in the coma, assumed later the "Cheyne-Stokes" type. The extensive septic cystitis and marked septic pyelo-nephritis found after death would account for most of the above condition, but could hardly explain the conjugate deviation of the eyes to the right. The hæmorrhage found in the right half of the brain, though small, may possibly have been the cause of this. In my other cases pyæmia, combined in several instances with uræmia, was undoubtedly the cause of death.

## PROGNOSIS OF DISSEMINATED SCLEROSIS.

Do cases of disseminated sclerosis ever recover? It is an accepted fact that cerebral or spinal tissue once having been completely destroyed by disease is not regenerated; as a consequence, it would follow that a permanent recovery in an advanced case of disseminated sclerosis is not to be expected. However, in disseminated sclerosis, the axis-cylinders and motor cells—as previously shown—resist the destructive process till late. This peculiar preservation of the actual nerve-elements cannot fail but make one think that if only the disease would become quiescent fairly early, sufficient amount of repair might take place to admit of complete functional recovery.

One occasionally meets with examples of great and apparently permanent amelioration of symptoms. I have recently had an opportunity of seeing such a case at the Crumpsall

Workhouse Hospital. A man of 50 began six years ago with weakness in the legs and impairment of vision. A little later trembling on movement commenced in the hands. On admission he presented well-marked general intention tremor, the characteristic syllabic speech, and nystagmus. The tremor in the arms was so severe that he had to be fed; walking was impossible; to use his own expression, his legs were "like sticks under him"; there was some slight loss of control over the bladder and rectum; he suffered much from vertigo, had incontrollable attacks of laughing and crying, and there was some failure of the memory. During the last three years he has been steadily improving. He can now walk very well, though the gait is somewhat spastic with the bending forwards seen in paralysis agitans; there is slight nystagmus, obtained with difficulty, and only on lateral movements; there is just the suspicion of a tremor in the left hand on voluntary movement, the vertiginous attacks are much less marked, the memory and sight have improved, he is less emotional, and has now no bladder or rectal troubles. The knee-jerks are active, but no ankle-clonus is obtained.

Catsaras[1] publishes a case which he considers an example of true disseminated sclerosis undergoing complete cure. The patient, a lad of 18, presented when first seen marked intention tremor, paresis of the lower extremities, nystagmus, associated palsy of the eyes, a vague look, vertigo, apoplectiform and epileptiform attacks, and psychical disturbances. Speech, sensation, optic discs, and the bladder and rectal functions were normal. The symptoms all entirely disappeared and there was entire absence of any recurrence. The treatment adopted was the application of the cautery to the spine, hydropathy, and the administration of ergot and bromo-hydrate of quinine.

In a case, under the care of Charcot, related by Marie,[2] there was also apparent recovery. The patient, a boy of 14, showed very marked intention tremor all over but most prominent in the upper limbs, rigidity of limbs, nystagmus (history of diplopia), slow speech with difficult articulation, staggering gait, etc. The ocular symptoms and tremor disappeared completely, the

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[1] *Loc. cit.*, p. 69.

[2] *Revue de Méd.*, Paris, 1883, III., p. 551.

walking became more and more sure, until at twenty he appeared a fine, robust-looking lad with no other symptom than severe and frequent headaches. The knee-jerks were, perhaps, still exaggerated, but, if so, the exaggeration was only slight and hardly appreciable.

In these cases, if they be true examples of disseminated sclerosis, it is probable that there is an arrest of the sclerotic process before complete destruction of the nerve elements has taken place, followed possibly by a deposit of new myeline around the naked axis-cylinders. *Post-mortem* examinations on such cases, dying from other causes, would be exceedingly interesting and instructive.

The fact that such prolonged and lasting remissions, which are almost equivalent to cure, occasionally occur in disseminated sclerosis, is of special importance as regards prognosis.

Predictions as to duration of life are often difficult. The conditions of each case must be carefully considered: the appearance of cystitis, bedsores, bulbar paralysis, and apoplectiform attacks being especially unfavourable, while, on the other hand, remissions of course tend to prolong life. Recovery usually takes place after an apoplectiform seizure, but death may occur in one, and the disease is always aggravated by such attacks. Disseminated sclerosis is apt to make rapid progress during pregnancy, especially in the later stages, and after delivery. The outlook in children is exceedingly grave, and convulsions especially are of bad omen.

### TREATMENT OF DISSEMINATED SCLEROSIS.

*Therapeutical Treatment.*—There is no known drug as yet discovered which possesses a specific action in arresting the morbid process, or which shows any power to repair the previous damage. The treatment must, therefore, be largely symptomatic or experimental, and even here the results have not been very encouraging. Cases are, however, reported in which drugs markedly influenced the distressing symptoms. Grasset and Sarda[1] quote the case of a man of 43, who gave a history of transient embarrassment of speech, temporary left facial paralysis, vertigo, etc.; on admission he showed very marked

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[1] *Progrès Méd.*, 7 Juillet, 1888, 2. S., T. VIII., No. 27.

intention tremor of the upper limbs, slight paresis of the left limb, impairment of hearing on the left side, dyspnœa, no eye symptoms, and no scanning speech. The patient was given ten to twenty centigrammes of solanine daily. In four days the tremor had completely disappeared, and the dyspnœa was also greatly relieved, but the drug had no effect whatever on the disease itself. Solanine appears to have a narcotic action on the medulla and cord. Feris and Spitzka[1] found veratrum, in doses of half a milligramme every four hours, very effectual in checking the tremor—veratrine appears to increase the duration of each individual muscular contraction. Hypodermic injections of hyoscyamine, arsenic, and curare have also caused the tremor to disappear for a short time, and lastly, large doses of the bromides have occasionally been useful. Many of the above-mentioned drugs, however, have to be given in almost toxic quantities, their continued use produces a physiological indifference to their effect, and many of them are very depressing and disturb the digestive and other functions. Their administration, therefore, does not seem as a rule justifiable.

Silver nitrate, strychnine, ergot, barium chloride, and phosphorus have been the drugs most commonly employed in treatment aimed at the disease itself. The first two of these were administered to several of my cases, but no marked benefit appeared to be derived from them. In Moncorvo's[2] three cases, signs of hereditary syphilis were either observed or matters of history, and two of them were benefited by mercurials and iodide. Other published cases, however, in which a history of syphilis, congenital or acquired, was present, showed no improvement under antisyphilitic treatment. Cod-liver oil, iron and quinine, has sometimes been of great use, especially in children. In an apparently typical case of disseminated sclerosis in a girl of eight, published by Wilson,[3] the administration of such tonic treatment was followed by a marked remission of symptoms.

*Mechanical Treatment.*—Motschutkousky[4] has tried suspension without any improvement in disseminated sclerosis.

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[1] *Loc. cit.*

[2] *Rev. Mens. d. mal. de l'enf.* Paris, 1887, V., p. 241.

[3] *Brit. Med. Jour.*, 1876, II., p. 675.

[4] *Brain*, Vol. XII., 1889, p. 338.

Arce Penalva[1] relates the case of a boy, aged 4 years, presenting symptoms of disseminated sclerosis, treated by a modification of the suspension apparatus used in tabes. The modification consisted in the addition of a weight to each limb, which he claimed hastened and increased the beneficial effects of suspension. Such modification would, however, materially increase the dangers of suspension, and should be adopted with extreme care, if at all. M'Culloch[2] tried stretching of both sciatic nerves with a force of twenty-four pounds in two typical cases of disseminated sclerosis, and states that both cases showed great immediate and permanent improvement.

*Electric Method.*—With the German school of neurologists electricity in the form of galvanism is a routine measure of treatment. Where there was muscular atrophy, faradism has been adopted. Very decided improvement has been stated to follow in some instances. In the case of a girl, published by Humphreys,[3] tremor disappeared for one month following the use of galvanism, though the symptoms all returned afterwards, and remained uninfluenced by any treatment.

*Hydropathy* has also had an extensive trial, but has not been found of much avail.

It seems to me that we can do little more for this, at present almost hopeless, disease, than maintain the patient's strength by careful dieting and administration of tonics; endeavour to prevent the formation of bedsores; and, if catheterism be required, to observe the most scrupulous aseptic precautions.

The important etiological relationship of acute infectious diseases to disseminated sclerosis suggests that possibly something might be done in the way of prophylaxis.

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[1] *Deutche med.-Zeit.*, Berlin, August 28, 1890.

[2] *Lancet*, II., 1885, p. 443.

[3] *Loc. cit.*

John Heywood, Excelsior Printing and Bookbinding Works, Manchester.